The New England
Journal of Medicine

Copyright, 1944, by the Massachusetts Medical Society

Volume 231 SEPTEMBER 28, 1944 Number 13

# ABNORMAL CARBOHYDRATE METABOLISM IN HUMAN THERMAL BURNS*

## Preliminary Observations

F. H. L. Taylor, Ph.D.,† Stanley M. Levenson, M.D.,‡ and Margaret A. Adams, A.B.§

BOSTON

UNTIL the last few years shock has been apparently the major cause of death in the first few days following severe burns. It is now well established that it can be prevented or successfully treated in most patients if they are seen soon enough after thermal injury. There are, however, still many early deaths among severely burned patients, despite the fact that clinical shock has not existed at any time or, if present, has been corrected. A series of investigations on the biochemical and physiologic changes occurring after thermal burns are being carried out with the view of determining the significance and therapeutic implications of these changes. The present communication is concerned with the preliminary observations on changes in carbohydrate metabolism and, to a lesser extent, with changes in nitrogen metabolism. Electrolyte studies carried out on these patients will be reported later.

Hyperglycemia occurring soon after burns has been reported in human beings by Davidson,[1] Underhill et al.,[2] Martin[3] and McIver.[4] In general, the rise in blood sugar was proportional to the severity of the burn. Many patients with minor burns showed no hyperglycemic response. The blood-sugar level in most cases returned to normal in twenty-four to forty-eight hours.

Lundberg and Backman[5] and Slocum and Lightbody,[6] working with burned rabbits, and Lambret, Driessens and Warembourg,[7] working with burned dogs, found similar results. The rise in blood sugar occurred within an hour after injury. The height and duration of the hyperglycemia was proportional to the severity of the burn. Thus, Lundberg and Backman report that in first-degree burns the blood sugar may increase to a level as high as 172 mg. per 100 cc. thirty minutes after the burn; at the end of two hours the level was again normal. Animals with second-degree burns showed rises of the blood-sugar level as high as 215 mg. and it returned to normal at the end of seven hours. With third-degree burns, the level rose to 326 mg. and at the end of twenty-four hours the blood sugar was still at an elevated level (154 mg.).

Greenwald and Eliasberg[8] reported hypoglycemia in 2 patients studied for the first time two and five days, respectively, following the burn injury. From their studies on burned rabbits they suggest that an early hyperglycemic phase is followed by a phase of hypoglycemia, but their data on this point are not convincing. Trusler et al.,[9] working with fatally burned dogs, found low blood-sugar values twenty-four hours after burning. Earlier determinations were not done.

Thomsen[10] and Wolff, Elkinton and Rhoads[11] have each reported 3 patients with moderately severe burns who showed impaired tolerance for glucose shortly after the injury. There was a gradual return to normal in the course of some days or even weeks.

The most recent study of carbohydrate metabolism following burning has been carried out by Clark and Rossiter.[12] Working with rabbits and rats, under ether anesthesia, these authors found an immediate rise in blood sugar after burning and a return to normal within twenty-four hours. The effect of the anesthetic was controlled. In rats, there was an increased blood lactic acid one hour but not three hours after burning. The blood lactic acid was not studied in rabbits. There was a slight decline in the carbon dioxide combining power in both rats and rabbits. In rats there was a fall in muscle glycogen but not in liver glycogen. In rabbits there was no change in liver glycogen in well-fed animals, but in animals starved for twenty-four hours there was a decrease. Muscle glycogen was not studied in rabbits. Liver slices from rab-

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) and the Burns Assignment of the Surgical Services, Boston City Hospital, and the Department of Medicine, Harvard Medical School.

The work described in this paper was done in part under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University.

Presented, in part, before the meeting of the Subcommittee on Burns and Wound Infections, National Research Council, Washington, D. C., March 31, 1944.

†Research associate in medicine, Harvard Medical School; chemist, Thorndike Memorial Laboratory, Boston City Hospital.

‡Research associate in surgery, Boston City Hospital.

§Laboratory assistant, Thorndike Memorial Laboratory, Boston City Hospital.

bits showed an impaired ability to form glycogen from glucose, whereas glycogen breakdown by liver pulp was unchanged.

## Methods of Study

The present report is based on studies of 35 consecutive patients with burns admitted to the Boston City Hospital during the last six months. There were no known diabetic patients in this group. The burns were treated locally with pressure dressings of dry sterile gauze, with no preliminary cleansing. Morphine sedation was given.

Samples of venous blood taken without stasis — usually from the femoral vein — were obtained on admission and at frequent intervals thereafter. The patients were admitted between one and two hours after the burn trauma. Any delay in admission beyond two hours is commented on in the appropriate place in the text.

Blood sugar was determined by two methods — one that of Folin,[13] and the other a modified Benedict procedure[14,15] following the removal of proteins by Somogyi's zinc sulfate method,[16] the final dilutions being made in Rothberg Evans tubes.[17] This second procedure greatly lessens the amount of non-glucose reducing substance in the filtrate, a matter of importance in determining "glucose" in the presence of hemoconcentration and hemolysis of red cells.[18]

A patient was presumed to have hyperglycemia when the Folin blood sugar exceeded 130 mg. per 100 cc., or the modified Benedict blood sugar 100 mg. Sugar tolerances were determined by the intravenous technic of Lozner et al.[19] Insulin-tolerance tests were made by the intravenous injection of 0.1 unit of regular insulin for each kilogram of body weight. Lactic acid was determined by the method of Barker and Summerson,[20] and amino acids by the ninhydrin method of Van Slyke et al.[21, 22] The carbon dioxide combining power, plasma proteins and chlorides were determined by the usual routine methods, as outlined by Peters and Van Slyke.[23] The serum sodium was determined by the method of Butler and Tuthill,[24] as modified by Consolazio and Dill.[25] Prothrombin times were determined by a modification[26] of Quick's[27] method. Cephalin flocculation tests were made by the method of Hanger.[28]

Shock was evaluated by the usual clinical criteria of fall of blood pressure, high pulse rate, cold, clammy extremities and collapse.

Several patients were treated with therapeutic plasma from the Boston City Hospital Blood Bank. Since this plasma contains glucose in amounts varying from 10 to 17 gm. for each unit of 250 cc., it was necessary to control this factor. This was accomplished in two ways. First, in certain moderately burned patients plasma was withheld; second, other patients were treated with either glucose-free plasma obtained through the kindness of Captain L. R. Newhouser, of the National Naval Medical Center, Washington, D. C., or glucose-free serum obtained by courtesy of Dr. Stephen Maddock, director of the Boston City Hospital Blood Bank. No protein, fat, carbohydrates or vitamins were given during the period of study, with exceptions that are specifically mentioned below.

## Results

### *Incidence of Hyperglycemia*

The over-all admission picture on the 35 patients comprising this study is given in Table 1. Twenty-one patients were in a hyperglycemic state on entry. The initial Folin blood-sugar level varied from 132 to 352 mg. per 100 cc. One patient whose admission was delayed twelve hours had an initial level of 224 mg.

Hemoconcentration was present on admission in 14 patients, 13 of whom showed marked hyperglycemia. Of the 21 patients whose hematocrits were normal on entry, 10 showed a high blood-sugar level on admission. Although there was a close correlation between the incidence of hemoconcentration and that of hyperglycemia, fluctuations in the hematocrit were not, for the most part, paralleled by similar changes in the blood sugar, nor did the non-glucose reducing substances, as a rule, vary directly with the degree of hemoconcentration.

Six patients with burns involving 20 to 75 per cent of the body surface, chiefly of third degree, were admitted in clinical shock. All these patients showed hyperglycemia, the blood sugar ranging from 168 to 352 mg. per 100 cc.

The occurrence of hyperglycemia was directly related to the extent of the burn. Thus, of 9 patients admitted with 2 to 9 per cent of the body surface burned, 2 had hyperglycemia. Of 7 patients admitted with 10 to 19 per cent of the body surface burned, 4 showed marked increases in the blood sugar on admission. On the other hand, 19 patients had more than 20 per cent of the body surface burned, and of these 15 showed marked hyperglycemia.

There is an even more striking correlation of the initial hyperglycemia with the extent of third-degree burn. Sixteen patients were admitted with less than 10 per cent of the body involved with third-degree burns. Of these, 4 showed hyperglycemia, 1 of whom was admitted in shock. In contrast to this incidence, 17 of 19 patients who had third-degree burns on more than 10 per cent of the body surface showed an initial increase in blood sugar. The 2 patients in this group who are not classified as having hyperglycemia had blood-sugar levels at the extreme upper limits of normal.

The data show no correlation of hyperglycemia with previous nutritional status, age, sex or abnormalities in the body temperature on admission.

*Duration of Hyperglycemia*

The foregoing evidence demonstrates that hyperglycemia occurring shortly after injury is a characteristic finding in severely burned patients. The hyperglycemia persisted over a period of hours in all cases, and over a period of days in some. None of the patients studied showed a return of an elevated blood-sugar level to normal within twelve hours.

The effect of a moderately severe burn on the blood sugar is demonstrated by a study of the data of one patient (Fig. 1).

Case 18. A 58-year-old woman, with a noncontributory past history, shortly before entry received flame burns on 15 per cent of the body surface, 10 per cent being third degree. The blood pressure and pulse were normal on entry and remained so during the first twenty-four hours. Plasma was withheld and 1500 cc. of isotonic salt solution was administered intravenously, but no other parenteral fluids were given. The oral intake during the period of study was limited to water. The urine output was moderately reduced on the first day but became normal thereafter. The blood-sugar level on admission was 133 mg. per 100 cc. Thereafter it rose, to a maximum of 238 mg. twenty hours after the burn. By that time the hematocrit, which had been normal on entry, had risen to a maximum of 51 per cent. Thereafter, both the hematocrit and the Folin blood sugar declined, the former reaching a normal value fifty hours after the injury. At that time, however, the blood-sugar level was 162 mg., and seventy-two hours after the burn was 141 mg.

*Carbon Dioxide Combining Power and Lactic Acid Level*

Plasma carbon dioxide combining power and lactic acid determinations were made on 15 patients. The 4 patients with third-degree burns on less than 10 per cent of the body surface had plasma carbon dioxide combining powers above 20 millimol. per liter on entry and plasma lactic acid concentrations of between 2.8 and 3.3 milliequiv. per liter. Of the 11 patients with third-degree burns involving more than 10 per cent of the body surface, 6 had carbon dioxide combining powers below 20 millimol. per liter, the lowest value being 13.6 millimol. The lactic acid concentration was between 2.8 and 3.3 milliequiv. in 2 patients, between 4 and 5 milliequiv. in 2, and 6.5 milliequiv. in 8. Thus, as in the case of the initial hyperglycemia, there was a close correlation between the initial decrease in carbon dioxide combining power, lactacidemia and the extent of the third-degree burn.

The following case reports illustrate the course and duration of the changes in lactic acid level and carbon dioxide combining power.

Case 2. The patient was a well-developed and well-nourished 33-year-old woman with a noncontributory past history who

Table 1. *Summary of Data.*

| Case No. | Age | Sex | Nutritional Status | Type of Burn | Extent of Burn: total | Extent of Burn: 3rd degree | Interval between Burn and Initial Blood Sampling | Initial Blood Sugar (Folin) | Initial Hematocrit | Initial Shock | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | % | % | hr. | mg./100cc. | % | | |
| 1 | 14 | F | Good | Hot aqueous fluid | 6 | 0 | 3 | 117 | 36 | 0 | Living |
| 2 | 33 | F | Good | Flame | 30 | 2 | 1 | 127 | 45 | 0 | Living |
| 3 | 40 | M | Fair | Flame | 75 | +++ | 2 | 269 | 47 | + | Died in 3 hr. |
| 4 | 16 | F | Good | Hot aqueous fluid | 6 | 0 | 1 | 93 | 38 | 0 | Living |
| 5 | 8 | F | Fair | Hot aqueous fluid | 10 | +− | 1 | 268 | 38 | 0 | Living |
| 6 | 45 | M | Fair | Hot aqueous fluid | 45 | +− | 1 | 206 | 65 | + | Died in 3 hr. |
| 7 | 49 | F | Good | Flame | 35 | +++ | 12 | 224 | 65 | + | Died in 7 days |
| 8 | 1 | F | Good | Hot aqueous fluid | 4 | 0 | 1 | 112 | 39 | 0 | Living |
| 9 | 7 | M | Good | Flame | 8 | 2 | 1 | 116 | 40 | 0 | Living |
| 10 | 54 | M | Fair | Flame | 20 | 15 | 3 | 201 | 53 | 0 | Died in 26 days |
| 11 | 53 | M | Good | Hot aqueous fluid | 6 | 0 | 1 | 103 | 40 | 0 | Living |
| 12 | 1 | F | Good | Hot aqueous fluid | 2 | 0 | 1 | 138 | 37 | 0 | Living |
| 13 | 50 | F | Fair | Hot aqueous flame | 10 | 10 | 2 | 142 | 44 | 0 | Died in 11 days |
| 14* | 42 | F | Good | Flame | 75+ | +++ | 1 | 202 | 49 | 0 | Died in 8 hr. |
| 15 | 48 | M | Fair | Flame | 15 | 15 | 1 | 163 | 41 | 0 | Living |
| 16 | 2½ | M | Fair | Hot aqueous fluid | 20 | 15 | 3 | 168 | 40 | + | Living |
| 17 | 62 | M | Good | Contact hot metal | 8 | 2 | 1 | 141 | 47 | 0 | Living |
| 18 | 58 | F | Fair | Flame | 15 | 10 | 2½ | 133 | 44 | 0 | Living |
| 19 | 3½ | M | Good | Hot aqueous fluid | 10 | 5 | 1 | 118 | 41 | 0 | Living |
| 20 | 38 | F | Good | Flame | 35 | 25 | 2 | 130 | 52 | 0 | Living |
| 21 | 2½ | M | Good | Flame | 5 | + | 1 | 84 | 39 | 0 | Living |
| 22 | 3 | M | Good | Hot aqueous fluid | 20 | 0 | 2 | 111 | 41 | 0 | Living |
| 23 | 5 | F | Good | Flame | 10 | ++ | 1 | 86 | 42 | 0 | Living |
| 24 | 32 | M | Fair | Flame | 7 | 2 | 1 | 110 | 47 | 0 | Living |
| 25 | 12 | F | Good | Flame | 20 | 15 | 1 | 132 | 41 | 0 | Living |
| 26 | 4 | M | Good | Flame | 50 | 40+ | 2 | 347 | 51 | 0 | Died in 63 hr. |
| 27 | 38 | F | Fair | Flame | 50 | +++ | 2 | 242 | 38 | 0 | Died in 63 hr. |
| 28* | 29 | M | Good | Electrical and flame | 35 | ++ | 1 | 172 | 58 | 0 | Died in 22 hr. |
| 29* | 3 | F | Good | Flame | 70 | +++ | 1½ | 352 | 38 | + | Died in 6 hr. |
| 30 | 45 | M | Fair | Flame | 20 | 15 | 2 | 164† | 51 | 0 | Died in 5 days |
| 31 | 75 | M | Fair | Flame | 20 | ? | 3 | 109 | 45 | 0 | Living |
| 32 | 8 | F | Good | Flame | 50 | ++ | 3 | 266 | 56 | 0 | Died in 66 hr. |
| 33* | 42 | F | Good | Flame | 15 | 10 | 3 | 100† | 40 | 0 | Living |
| 34* | 45 | M | Good | Flame | 60 | +++ | ½ | 150† | 52 | 0 | Died in 16 hr. |
| 35 | 83 | M | Fair | Hot aqueous fluid | 35 | ++ | 2 | 220† | 45 | + | Died in 22 hr. |

* Respiratory involvement.
†Benedict blood sugar.

1 hour before entry received flame burns on 30 per cent of the body surface. For the most part, the burns were deep second degree, only 2 per cent being third degree. The blood

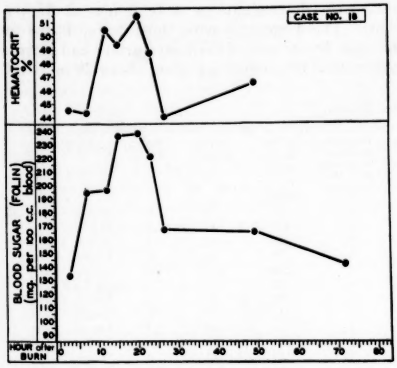


FIGURE 1.

pressure, pulse, temperature and respirations were normal on entry and remained so during the period of study. During the first 24 hours she received 3000 cc. of isotonic salt solution by clysis; plasma was withheld, and no other parenteral fluids were given. The oral intake of water and the urine output were low on the 1st day but normal in amount thereafter. The significant laboratory findings are presented in Figure 2.

The hematocrit, which was normal on entry, rose slowly during the first 19 hours, reaching a level of 56 per cent. From then on there was a slow decline to 41 per cent on the 3rd day, at about which level it remained. During that time the plasma protein concentration, which had been normal on entry, gradually fell 4.4 gm. per 100 cc. at the end of 39 hours, presumably owing to a shift of interstitial fluid into the blood stream. The nonprotein nitrogen fluctuated between 35 and 43 mg. during the first 39 hours and fell to 28 mg. at 63 hours.

The blood lactic acid level 2 hours after the burn was elevated to 2.8 milliequiv. per liter. During the next 6 hours it was within normal limits, but during the next 28 hours the concentration varied from 2.0 to 3.9 milliequiv. Further serial studies were not made, but a blood lactic acid determination on the 7th day was normal.

The carbon dioxide combining power of the plasma during the first 63 hours varied between 18 and 24 millimol. per liter. Thereafter, the values remained at 28 millimol. Therefore, during the early period following injury there was apparently a slight but definite decrease in the carbon dioxide combining power.

The blood-sugar level as determined by the Folin method was normal on entry and as determined by the Somogyi-Benedict method was slightly elevated. It gradually rose, the maximum hyperglycemia being observed at 8 hours, with values of 197 mg. by the Folin method and 150 mg. by the Somogyi–Benedict method. The rise in the blood sugar and in the non-glucose reducing substances did not parallel the hematocrit. Thereafter there was a slow decline in the blood sugar over a period of 3 days. No glucose-tolerance tests were done on this patient until the 5th day after the injury, at which time the tolerance was normal.

CASE 13. The patient was a 50-year-old woman whose past history was noncontributory except for moderate alcoholic intake. She received flame burns of 10 per cent of the body surface shortly before entry. The entire burn was deep third degree, the injured skin being completely charred, with fat exposed in a number of places. The blood pressure, pulse and respirations were normal on entry and remained so during the period of study. Fifteen hundred cubic centimeters of physiologic salt solution was given by clysis, but no other parenteral fluids were given. The oral intake was restricted

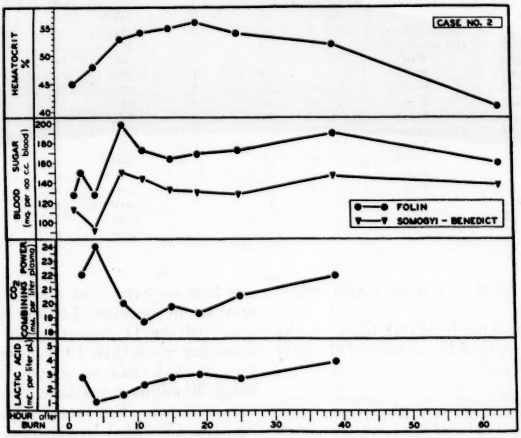
CASE NO. 2
HEMATOCRIT %
BLOOD SUGAR (mg. per 100 cc. blood)
FOLIN
SOMOGYI - BENEDICT
CO2 COMBINING POWER (mM. per liter plasma)
LACTIC ACID (mg. per liter pl.)
HOUR after BURN

FIGURE 2.

to a small amount of water during the first 36 hours. The urine output was low the 1st day but normal thereafter. The data on this patient are given in Figure 3.

The hematocrit on entry was 44 per cent, at which level it remained for the first 14 hours. There was a slow decline to 34 per cent at the end of 3 days.

The plasma nonprotein nitrogen rose from a level that was initially normal to 75 mg. per 100 cc. 22 hours after the burn was sustained. It declined slowly and reached a level of 39 mg. 65 hours after the injury, at which level it remained. The plasma protein was 6.1 gm. per 100 cc. on entry and declined

slowly to 5.2 gm. in 3 days. On this basis, there was comparatively little interstitial fluid exchange in this patient.

Hyperglycemia, although present, was less marked than in Case 2. The blood sugar rose earlier and reached a peak moderate and the nonprotein nitrogen remained normal, but a marked hyperglycemia, by both the Folin and the Somogyi–Benedict method, was present. The blood-sugar reached a level of 288 mg. per 100 cc. by the former method

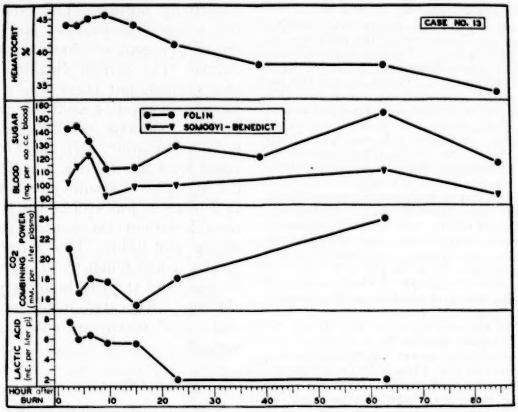
CASE NO. 13
HEMATOCRIT %
BLOOD SUGAR (mg. per 100 c.c. blood)
FOLIN
SOMOGYI - BENEDICT
CO2 COMBINING POWER (mM. per liter plasma)
LACTIC ACID (mE. per liter plasma)
HOUR after BURN

FIGURE 3.

of 144 mg. per 100 cc. by the Folin method and 122 mg. by the Benedict method between 3 and 5 hours after the injury. The level thereafter was normal except for a transitory rise at 62 hours. A glucose-tolerance test done on the 4th day was normal.

In contrast to the relatively slight rise in blood sugar, there was soon after the injury a marked lactacidemia. On entry, 1 hour after the burn, the blood lactic acid level was six times as high as the normal level, namely, 7 milliequiv. per liter. A high lactic acid level persisted for 14 hours, after which it slowly declined, reaching a relatively normal value in 62 hours.

The carbon dioxide combining power of the plasma, which was 21.4 millimol. per liter on admission, declined to 15.5 millimol. 12 hours later. Thereafter it slowly rose, reaching a level of 26.8 millimol. 62 hours after the burn.

The above two cases are typical of the findings in moderately burned patients, who, in our experience, usually recover from their injury. The following two cases represent patients who had much severer burns and who did not survive the injury.

CASE 14. The patient was a 42-year-old Negress who shortly before entry received flame burns when an oil stove exploded. No further history could be obtained. Physical examination on admission revealed a well-developed and well-nourished woman in moderate distress. The systolic blood pressure was 120, the pulse 90, and the respirations 20. After the burns were dressed it was not possible to take blood-pressure readings, but from the quality of the femoral pulse and the patient's general appearance it did not appear that any profound peripheral failure was present. She died 8 hours after injury from respiratory failure. Fifteen hundred cubic centimeters of plasma, containing about 75 gm. of glucose, was given in the period from 3 to 6 hours after entry. No other fluids were given parenterally or by mouth. There was marked hemoglobinemia. Five hundred cubic centimeters of clear urine was obtained on entry, but none thereafter. The rectal temperature varied from 102 to 102.8°F.

Three sets of observations were made and are summarized in Figure 4. The first two were made before any plasma or glucose had been given. Hemoconcentration was only and of 241 mg. by the latter at the time of the last observations.

The carbon dioxide combining power of the plasma, which

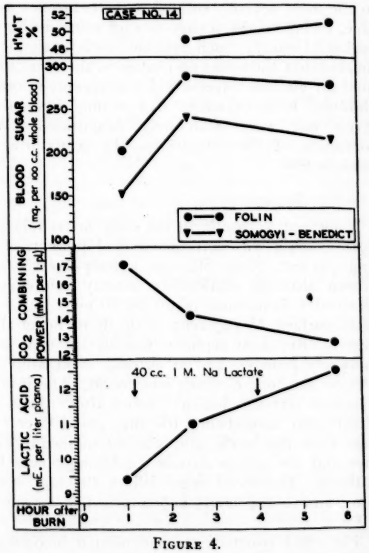
CASE NO. 14
H'M'T %
BLOOD SUGAR (mg. per 100 c.c. whole blood)
FOLIN
SOMOGYI - BENEDICT
CO2 COMBINING POWER (mM. per L. pl.)
LACTIC ACID (mE. per liter plasma)
40 cc. 1 M. Na Lactate
HOUR after BURN

FIGURE 4.

was 17.1 millimol. per liter on entry, fell to 12.5 millimol. in the next 4 hours.

The plasma lactic acid on entry was considerably elevated, a value of 9.4 milliequiv. per liter being obtained. During the next 4 hours the patient received a total of 80 cc. of 1.0 molar lactate and the lactic acid level rose to 12.5 milliequiv.

CASE 29. The patient was a 3-year-old Negress with a noncontributory past history who shortly before entry received third-degree flame burns on 70 per cent of the body surface, together with respiratory damage. Examination on entry revealed a well-developed and well-nourished child who was comatose, with labored respirations. The pulse was 160 and weak, and the extremities were cold and clammy. The clinical condition improved on the administration of oxygen and 600 cc. of plasma. The pulse became stronger and slower and the extremities warm. A Levine tube was passed into the stomach at the 2nd hour after the burn and bloody fluid was obtained. Small amounts of water were administered by gavage. On catheterization at the 5th hour 5 cc. of dark-red urine was obtained The rectal temperature rose to 105°F. The respirations became more labored, and a tracheotomy was performed 3 hours after injury, with marked alleviation of the respiratory distress. Three hours later, however, the patient suddenly developed respiratory spasm and died.

The hemoglobin varied from 89 to 92 per cent, with the highest value 3 hours after the injury. (These values are higher than those usually found in children in this hospital and probably indicate hemoconcentration.)

The plasma nonprotein nitrogen on entry was 30 mg. per 100 cc. and by the 5th hour had risen to 89 mg.

The carbon dioxide combining power on entry was 13.6 millimol. per liter. During the next 4 hours, 50 gm. of glucose was given intravenously in divided doses. The blood sugar remained at a very high level, the highest value being 700 mg. per 100 cc. 2 hours after the last administration of glucose.

The blood lactic acid on entry was markedly elevated, being 7.2 milliequiv. per liter. Five hours after the burn injury it had risen to 10 milliequiv. No sodium lactate was administered.

Data with respect to glycosuria and acetonuria in the most severely burned patients are not available, owing to the scanty flow of urine during the period of study. Such evidence as is available indicates that there was no change in the renal threshold for glucose. Acetonuria was present in only 2 children, both of whom had normal blood-sugar levels but were moderately dehydrated. With correction of the dehydration the acetonuria disappeared.

*Insulin Tolerance*

Tolerance to insulin in the early hours following burn trauma was determined in 3 patients. The first patient, (Case 30) was a forty-five-year-old, known alcoholic addict who shortly before entry received a flame burn involving 20 per cent of the body surface, 15 per cent of the burn being third degree. Repeated cephalin flocculation tests were markedly positive, and at autopsy moderately advanced alcoholic cirrhosis was found. The insulin-tolerance test was begun 3 hours after injury, the blood-sugar level being 168 mg. per 100 cc. At that time the lactic acid was 6.6 milliequiv. per liter and the carbon dioxide combining power 19.2 millimol. The blood sugar fell to 108 mg. in one hour, and in two hours had returned to a value of 138 mg.

The other two patients had normal blood-sugar levels at the time the insulin-tolerance test was made. One of these (Case 31) was a seventy-five-year-old man who had burns on 20 per cent of the body surface, chiefly deep second degree. During the test he showed mild transient shock. The lactic acid level and carbon dioxide combining power were essentially normal. The other patient, (Case 33) was a forty-two-year-old Negress with flame burns on 15 per cent of the body surface, chiefly third degree. The carbon dioxide combining power was also normal, but there was slight elevation of the lactic acid level (4 millimol. per liter). Both these patients showed marked insulin sensitivity five hours after injury. In the first, the control blood-sugar level was 97 mg. per 100 cc. One hour after the injection of insulin it had fallen to 66 mg., and at 2 hours it was still at the level of 60 mg. In the second patient the control blood-sugar level was 98 mg. per 100 cc. One hour after the injection of insulin it had fallen to 49 mg. and by two hours to 39 mg., and at three hours it was still at a low level (24 mg.) Repeated insulin-tolerance tests on the ninth and seventy-seventh days were essentially normal.

*Glucose Tolerance*

The interpretation of early glucose-tolerance tests in these patients is difficult because of the spontaneous changes in blood sugar. In some of the patients with hyperglycemia, however, it appeared that the *added* glucose was utilized; that is, the blood sugar two hours after the injection of glucose was the same as, or lower than, the control value. This is illustrated by the following three patients, one of whom was a well-nourished girl who was in good clinical condition at the time of the test. The second was a well-nourished young man in shock at the time of the test, and the third was an alcoholic addict with liver disease but without evidence of clinical shock.

CASE 25. The patient was a 12-year-old Negress with a noncontributory past history who shortly before entry received deep third-degree burns on 15 per cent of the body surface, an additional 5 per cent being involved in second-degree burns. Examination revealed a well-developed and well-nourished girl. The temperature, blood pressure, pulse and respirations were normal on admission. During the first 12 hours the patient received 750 cc. of glucose-free plasma and 360 cc. of water by mouth. There was no vomiting. The urine output was low. The blood pressure remained at about 120/80, the pulse was 110, and the general condition was good. The hematocrit rose from 41 to 47 per cent, whereas the plasma protein concentration remained at about 6.4 gm. per 100 cc. The plasma nonprotein nitrogen rose from 28 to 33 mg. per 100 cc. The carbon dioxide combining power of the plasma varied between 22 and 26 millimol. per liter. The lactic acid was elevated on entry, being 2.3 milliequiv. per liter, but fell to a normal value (0.8 milliequiv.) 12 hours after admission. The blood-sugar level on entry and again an hour later was 124 mg. per 100 cc. by the Somogyi–Benedict method. Twenty-five grams of glucose was injected intravenously at that time, and 2 hours later the blood-sugar level was still 124 mg. Thereafter it was normal. A glucose-tolerance test on the 3rd day was normal.

CASE 28. The patient was a 29-year-old man who received flame and electrical burns and some damage to the respiratory tract. Thirty-five per cent of the body was involved in second-degree and third-degree burns. On entry the blood

pressure was 130/70, the pulse was 100 and of good quality and the respirations were 25. The temperature during the first 5 hours was 103.6°F. Water in sips was the only fluid given. Plasma was withheld. During that time the patient gradually went into profound circulatory collapse, no blood pressure or pulse being obtainable for the last half-hour. There was no output of urine. The hematocrit rose to 72 per cent, and the plasma lactic acid concentration to 5 milliequiv. per liter. The blood-sugar level, which had been normal on admission, rose to 190 mg. per 100 cc. within 1 hour. A glucose-tolerance test was begun at that time. Two hours later the blood-sugar level was 157 mg.

Case 27. The patient was a 38-year-old woman with probable liver disease who 1 hour before entry received third-degree flame burns on 50 per cent of the body surface. She was a known morphine and alcoholic addict. Physical examination revealed a well-developed and well-nourished woman. The blood pressure, pulse and respirations remained normal during the period of study. The plasma icteric index was 20 to 25 units. There was moderate hemoconcentration, lactacidemia and hyperglycemia. The carbon dioxide combining power varied between 18 and 20 millimeters per liter. A glucose-tolerance test was done at 4 hours. The control blood-sugar level was 286 mg. per 100 cc. Two hours after the injection of the glucose the level was 204 mg.

Glucose-tolerance tests on 4 patients after the fourth day were normal. Two of these patients had shown hyperglycemia, lactacidemia and lowered carbon dioxide combining power during the first two days, whereas the other patients had normal blood-sugar levels but had shown sensitivity to insulin.

*Oxygen Consumption*

Oxygen consumption was determined in 3 patients (Cases 28, 30 and 33) twelve to thirteen hours after injury. Calculated in terms of basal metabolic rates, the results varied from +34 to +58 per cent. The temperature in each case at the time of the determination was 103° F.

*Icteric Index*

In 23 patients the icteric indices were normal, whereas in 2 patients (Cases 27 and 30), both known alcoholic addicts, the index was elevated to 12 to 15 and 20 to 25 units, respectively. Of the remaining 10 patients, no data are available on 3; in the 7 others — all with burns involving more than 35 per cent of the body surface — the icteric index could not be estimated because of the presence of marked hemoglobinemia.

*Cephalin-Flocculation Test*

Serial cephalin-flocculation tests were made on 6 patients, all with third-degree burns involving more than 15 per cent of the body surface. In 3 patients (Cases 31, 32 and 33), the tests were negative, or at the most slightly positive (+). The icteric indices of these patients were normal. In the other 3 patients, 2 (Cases 30 and 34) of whom were known alcoholic addicts, and the third (Case 35) a poorly nourished man of eighty-three, the test was strongly positive (+++ to ++++) throughout their courses. In two of these patients the icteric indices were not determined because of the presence of hemoglobinemia. In the third patient it was elevated to 15 units.

*Prothrombin Time*

Serial prothrombin determinations were made on the same 6 patients in whom the cephalin flocculation was studied. Of the 3 with negative cephalin-flocculation tests, 2 (Cases 31 and 33) showed normal prothrombin concentrations and 1 (Case 32) showed slight prolongation eighteen hours after the burn. Of the 3 with positive cephalin-flocculation tests, 2 (Cases 30 and 34) showed moderate prolongation four and forty-one hours, respectively, after the burn.

## Discussion

From the data presented it is clear that hyperglycemia, lactacidemia and lowered carbon dioxide combining power are frequently found in human subjects following thermal injury. The extent and duration of the changes in these blood constituents are roughly proportional to the severity of the burn. Muscle and liver glycogen determinations were not made in these patients; however, Clark and Rossiter,[12] working with rats, and Greenwald and Eliasberg,[8] working with rabbits, found decreases in the muscle glycogen following burns. Clark and Rossiter found no change in liver glycogen in rats and rabbits previously well fed, whereas in rabbits previously starved there was a decrease. Following burn injury, there was no significant degree of early liver damage in those patients treated with simple dressings who came to autopsy in this hospital. The few patients who showed clinical and laboratory evidence of liver damage had a long history of alcoholism and doubtless had liver damage previous to the burn. In 1 patient with such presumptive evidence, the liver was found at autopsy to be markedly cirrhotic. It appears, therefore, that in the presence of a normal liver any increase in lactic acid production due to an increase in the rate of muscle glycogenolysis may result in hyperglycemia. The rate of lactic acid formation following burns is, however, apparently greater than the liver can handle, resulting in lactacidemia as well as hyperglycemia.

In addition to an increased glycogenolysis, another possible source of the extra blood sugar is glucogenesis from protein. It has been shown that following thermal burns there is an early increase in protein catabolism, with the excretion of excessive amounts of nitrogen in the urine.[29] It is quite possible that some of this protein is converted to glucose. Another possible factor is the moderate increase in metabolic rate that was found in a few cases in this study.

Hyperglycemia and lactacidemia are not peculiar to burn injury but have been reported following other types of trauma,[30,31] hemorrhagic shock,[32] acidosis,[33] anhydremia[34] and low oxygen tension.[35] The degree of acidosis, dehydration and oxygen lack

necessary to produce significant metabolic abnormalities, however, is such that these factors can only have been contributory factors in the cases presented here. Similarly, although hyperglycemia has been reported following the administration of morphine,[36-39] the amounts of the drug required in animals are relatively many times the dosage received by our patients. However, the fact that morphine can cause such a metabolic change should be kept in mind when considering the sedation of burned patients.

The changes in carbohydrate metabolism following hemorrhage are more applicable to the present investigation, since there are certain over-all similarities between burn shock and hemorrhagic shock. Following hemorrhage, Robertson[40] presented evidence in cats that the liver is the site of formation of the extra glucose: the sugar content of the hepatic vein blood was higher than that of the heart blood, and ligation of the hepatic vessels prior to bleeding prevented the hyperglycemia. Brooks[32] working with chronic spinal cats, showed that an intact sympathetic system is necessary for the production of the hyperglycemia. Of some interest is the fact that Govier[41] was able to reverse some of the effects of hemorrhage on carbohydrate metabolism in cats by the administration of large doses of thiamin chloride.

Most investigators working with burns have emphasized the role of the adrenal glands in the production of abnormalities in the carbohydrate metabolism. Hartman,[42] working with cats, found an increase in the circulating adrenaline, as measured by the pupil-dilatation test, and a depletion of the adrenaline content of the adrenal glands. Clark and Rossiter[12] have demonstrated some differences between the action of adrenalin and the effects of burn injury. The liver glycogen was increased in animals receiving adrenalin but not in burned animals, and, secondly, liver slices from burned rabbits did not readily form glycogen from glucose in vitro, whereas liver slices from animals receiving adrenalin were able to synthesize glycogen.

Browne[43] and Cope et al.[44] found increased 17-ketosteroid excretion in the first few days following burns, which was followed by a decrease below normal values. Greenwald and Eliasberg[8] working with rabbits, and Olbrycht,[45] Weiskotten[46, 47] and Mallory,[48] studying patients, have found adrenocortical hypertrophy and a marked depletion of the lipoids. When the burn was severe there was actual necrosis of the cortical cells.

Sayers et al.[49] state that in burns the adrenal glands are stimulated to exhaustion, and the degree of response is that described in their classification as Type III.

Adrenalectomy was found by Slocum and Lightbody[6] to prevent the lactacidemia but not the hyperglycemia in burned rabbits. Clark and Rossiter[12] found that adrenalectomy did not completely abolish the hyperglycemia and lactacidemia. It therefore appears that although the adrenal glands may play an important role in the production of abnormalities in carbohydrate metabolism following burns, the entire picture cannot be explained on this basis, and, indeed, the effect of the adrenal glands may be of a secondary nature.

Pathologic changes in other organs following burns have not been consistently found. With conservative surface treatment, which precludes the use of tannic acid and other substances, which have been found to produce focal necrosis, little or no pathologic change in the liver has been observed in our autopsy material. No specific lesions have yet been reported as occurring in the pancreas. The pituitary gland itself has not been studied, so far as an examination of the literature reveals, although Christophe[50] has described a so-called "burn lesion" in the brain. He found this lesion in the region of the hypothalamus following burning or even after the transfusion of blood from burned animals into the cerebral circulation of a normal animal.

From the foregoing, it appears that there are many possible explanations of the biochemical changes mentioned in this paper. Our own evidence does not permit any statement of the primary cause at the present time. It is not improbable that, whatever the cause is, increased glycogenolysis and possibly gluconeogenesis could have accounted for the findings presented here. It will be necessary to make studies of the actual muscle and liver glycogen reserves of the patients to gain support for this view.

It is already apparent in the small series of 35 patients presented in this report that a marked hyperglycemia associated with lactacidemia and acidosis go hand in hand with a poor prognosis. So, too, does the counterpart of these findings, namely, the presence of third-degree burns involving more than 25 per cent of the body surface.[51]

Although it may be argued that, in general, patients do not die from the biochemical changes reported here, nevertheless the effect of the burn trauma on the organism as a whole must indeed be profound in order to produce such changes in carbohydrate metabolism as are shown in Cases 14 and 29. In any event, from the therapeutic point of view it seems reasonable to suppose that the high blood sugar and lactic acid are obtained at the expense of the carbohydrate reserves of the body. Since in a few of the patients reported here added glucose could be metabolized in the face of a hyperglycemia, it seems reasonable to replace the depleted carbohydrate reserves by the administration of glucose, and to attempt by whatever means possible to increase, in the future, the utilization of carbohydrates by the burned patient. Such a therapeutic approach may well be of benefit.

## Summary

In a study of 35 consecutive burned patients, a high incidence of hyperglycemia, lactacidemia and a moderate reduction in the carbon dioxide combining power of the plasma were found.

There is a high degree of correlation between these abnormalities of carbohydrate metabolism and the severity of the burn.

The few glucose-tolerance tests that were made indicate that in some severely burned patients with hyperglycemia there remains a considerable ability to metabolize added glucose.

There was no evidence of liver damage in these patients as a result of the burn injury. In the few cases in which liver damage was found, it was present before the injury, being for the most part an alcoholic cirrhosis.

Some of the possible physiologic and pathologic bases for the abnormalities of carbohydrate metabolism following burns have been discussed.

The abnormalities in carbohydrate metabolism that have been presented are not inconsistent with the presence of an increased glycogenolysis, together with a possible gluconeogenesis from protein.

It is suggested that additional glucose be given early to burned patients.


We are indebted to Drs. George R. Minot and Charles C. Lund for the interest shown in the development of this work, and to Professor R. A. Peters of Oxford, England, for permitting us to examine the data of Clark and Rossiter prior to publication. The technical assistance of Miss Alice Ballou, Miss Dorothy Keller, Miss Mary Maloney, Miss Jeanette Maioli, Miss Gladys Roberts and Mr. Theodore Kisil, is gratefully acknowledged. Dr. George Bottomley kindly permitted us to include Case 32, which was under his clinical care. The clinical and metabolic records were the work of Miss M. Morrow and Miss A. H. MacDonald.

## References


1. Davidson, E. C. Tannic acid in treatment of burns. *Surg., Gynec. and Obst.* **41**:202-221, 1925.
2. Underhill, F. P., Carrington, G. L., Kapsinow, R., and Pack, G. T. Blood concentration changes in intensive superficial burns, and their significance for systemic treatment. *Arch. Int. Med.* **32**: 31-49, 1923.
3. Martin, J. D., Jr. Clinical and experimental studies of burns. *J. M. A. Georgia* **27**:39-46, 1938.
4. McIver, M. A. Study in extensive cutaneous burns. *Ann. Surg.* **97**: 670-682, 1933.
5. Lundberg, H., and Backman, E. L. Action des brulures sur la teneur du sang en glucose et en elements figurés. *Compt. rend. Soc. de biol.* **101**:931-934, 1929.
6. Sloan, M. A., and Lightbody, H. D. Changes in sugar and lactic acid content of blood caused by burns. *Am. J. Physiol.* **96**:35-39, 1931.
7. Lambret, O., Driessens, J., and Warembourg, H. Le syndrome humoral des brulures. *Compt. rend. Soc. de biol.* **123**:10, 1936.
8. Greenwald, H. M., and Eliasberg, H. Pathogenesis of death from burns. *Am. J. M. Sc.* **171**:682-696, 1926.
9. Trusler, H. M., Egbert, H. L., and Williams, H. S.: Burn shock, question of water intoxication as complicating factor: blood chemical studies and report of extensive burn treated by repeated transfusions of blood and blood plasma. *J. A. M. A.* **113**:2207-2213, 1939.
10. Thomsen, V. Studies of trauma and carbohydrate metabolism with special reference to existence of traumatic diabetes. *Acta Med. Scandinav.* Supp. 91: 367-389, 1938.
11. Wolff, W. A., Elkinton, J. R., and Rhoads, J. E. Liver damage and dextrose tolerance in severe burns. *Ann. Surg.* **112**:158-160, 1940.
12. Clark, E. J., and Rossiter, R. J. Carbohydrate metabolism after burning. *Quart. J. Exper. Physiol.* **32**:279-300, 1944.
13. Folin, O., and Wu, H. System of blood analysis: simplified and improved method for determination of sugar. *J. Biol. Chem.* **41**: 367-374, 1920.
14. Benedict, S. R. Determination of blood sugar. *J. Biol. Chem.* **64**: 207-213, 1925.
15. *Idem.* Estimation of sugar in blood and normal urine. *J. Biol. Chem.* **68**:759-767, 1926.
16. Somogyi, M. Method for preparation of blood filtrates for determination of sugar. *J. Biol. Chem.* **86**:655-663, 1930.
17. Rothberg, V. E., and Evans, F. A. Modified Folin and Wu blood sugar method. *J. Biol. Chem.* **58**:443-451, 1923.
18. Shen, S. C., Ham, T. H., and Fleming, E. M. Studies on destruction of red blood cells. III. Mechanism and complications of hemoglobinuria in patients with thermal burns: spherocytosis and increased osmotic fragility of red blood cells. *New Eng. J. Med.* **229**: 701-713, 1943.
19. Lozner, E. L., Winkler, A. W., Taylor, F. H. L., and Peters, J. P. Intravenous glucose tolerance test. *J. Clin. Investigation* **20**:507-515, 1941.
20. Barker, S. B., and Summerson, W. H. Colorimetric determination of lactic acid in biological material. *J. Biol. Chem.* **138**:535-554, 1941.
21. Van Slyke, D. D., Dillon, R. T., MacFadyen, D. A., and Hamilton, P. H. Gasometric determination of carboxyl groups in free amino acids. *J. Biol. Chem.* **141**:627-669, 1941.
22. Hamilton, P. B., and Van Slyke, D. D. Gasometric determination of free amino acids in blood filtrates by ninhydrin-carbon dioxide method. *J. Biol. Chem.* **150**:231-250, 1943.
23. Peters, J. P., and Van Slyke, D. D. *Quantitative Clinical Chemistry.* Vol. 2. Methods. 957 pp. Baltimore: Williams & Wilkins Company, 1932. Pp. 283-285.
24. Butler, A. M., and Tuthill, E. Application of uranyl zinc acetate method for determination of sodium in biological material. *J. Biol. Chem.* **93**:171-180, 1931.
25. Consolazio, W. V., and Dill, D. B. Determination of sodium. *J. Biol. Chem.* **137**:587-592, 1941.
26. Souter, A. W., and Kark, R. M. Quick's prothrombin test simplified by use of stable thromboplastin. *Am. J. M. Sc.* **200**:603-607, 1940.
27. Quick, A. J., Stanley-Brown, M., and Bancroft, F. W. Study of coagulation defect in hemophilia and in jaundice. *Am. J. M. Sc* **190**:501-511, 1935.
28. Hanger, F. M. Serological differentiation of obstructive from hepatogenous jaundice by flocculation of cephalin-cholesterol emulsions. *J. Clin. Investigation* **18**:261-269, 1939.
29. Taylor, F. H. L., Davidson, C. S., Levenson, S. M., and Adams, M. A. Abnormal nitrogen metabolism in patients with thermal burns. *New Eng. J. Med.* **229**:855-859, 1943.
30. Beard, J. W., and Blalock, A. Experimental shock: composition of fluid that escapes from blood stream after mild trauma to extremity, after trauma to intestines and after burn. *Arch. Surg.* **22**:617-625, 1931.
31. Gutmann, H., Olson, W. H., Kroll, H. H., Levinson, S. O., and Necheles, H. Chemical studies in traumatic shock. *Am. J. Physiol.* **133**:308, 1941.
32. Brooks, C. M. Reaction of chronic spinal animals to hemorrhage. *Am. J. Physiol.* **114**:30-39, 1935.
33. Guest, M. M., and Rawson, R. A. Carbohydrate storage and mobilization with changes in the blood pH. *J. Biol. Chem.* **139**:535-542, 1941.
34. Marriott, W. M. Anhydremia. *Physiol. Rev.* **3**:275-294, 1923.
35. Kellaway, C. H. Hyperglycemia of asphyxia and part played therein by suprarenals. *J. Physiol.* **53**:211-233, 1919.
36. Houssay, B. A., Lewis, J. T., Molinelli, E. A., and Marenzi, A. D. Etudes sur l'hyperglycémie consécutive à l'injection de morphine: rôle du sympathique. *Compt. rend. Soc. de biol.* **99**:1406, 1928.
37. Bodo, R. C., Cetui, F. W., and Benaglia, A. E. Mechanism of morphine hyperglycemia. *J. Pharmacol. & Exper. Therap.* **57**:115, 1936.
38. *Idem.* Studies on mechanism of morphine hyperglycemia: role of adrenal glands. *J. Pharmacol. & Exper. Therap.* **61**:48-57, 1937.
39. *Idem.* Studies on mechanism of morphine hyperglycemia: role of sympathetic nervous system with special reference to sympathetic supply to liver. *J. Pharmacol. & Exper. Therap.* **62**:88-105, 1938.
40. Robertson, J. D. Effect of hemorrhage of varying degree on blood and plasma volume, on blood sugar, and on arterial blood-pressure. *J. Physiol.* **84**:393-409, 1935.
41. Govier, W. M., and Greer, C. M. Studies on shock induced by hemorrhage; effect of thiamin on disturbances of carbohydrate metabolism. *J. Pharmacol. & Exper. Therap.* **72**:321-330, 1941.
42. Hartman, F. A., Rose, W. J., and Smith, E. P. Influence of burns on epinephrin secretion. *Am. J. Physiol.* **78**:47-49, 1926.
43. Browne, J. S. L. Personal communication.
44. Cope, O., Nathanson, I. T., Rourke, G. M., and Wilson, H. Symposium on management of Cocoanut Grove burns at Massachusetts General Hospital: metabolic observations. *Ann. Surg.* **117**:937-958, 1943.
45. Olbrycht, I. Étude expérimentale de la pathogénie de la morte par brûlure. *Rev. de med.* **41**:81-115, 1924.
46. Weiskotten, H. G. Fatal superficial burns and suprarenals: note on occurrence of suprarenal lesions in uncomplicated fatal cases of extensive superficial burns. *J. A. M. A.* **69**:776, 1917.
47. *Idem.* Histopathology of superficial burns. *J. A. M. A.* **72**:259-261, 1919.
48. Mallory, T. B., and Brickley, W. J. Symposium on management of Cocoanut Grove burns at Massachusetts General Hospital: pathology, with special reference to pulmonary lesions. *Ann Surg.* **117**: 865-884, 1943.
49. Sayers, G., Sayers, M. A., Fry, E. C., White, A., and Long, C. M. H. Effect of adrenotropic hormone of anterior pituitary on cholesterol content of adrenals. *Yale J. Biol. & Med.* **16**:361-392, 1944.
50. Christophe, L. Conception nouvelle de mécanisme de la mort des brulés. *Presse méd.* **46**:1054, 1938.
51. Clowes, G. H. A., Jr., Lund, C. C., and Levenson, S. M. Surface treatment of burns: comparison of results of tannic acid, silver nitrate, triple dye, and vaseline or boric ointment as surface treatments in 150 cases. *Ann. Surg.* **118**:761-779, 1943.

# WAR NEUROSIS*

SURGEON (R) SAMUEL H. EPSTEIN, U.S.P.H.S.†

BALTIMORE

DURING the last world war, military psychiatry constituted a major medical problem.[1] In the course of the postwar years, aggregating nearly a generation, the enormity of the nation's psychiatric problems became obvious to the Veterans Administration, to which the care of the last war's medical problems were entrusted. Since the beginning of the present war, much emphasis has been laid on psychiatry, not only from the standpoint of therapy but also in its preventive aspects. The term "shell shock," coined in the last war, was recognized as a functional nervous disorder and soon gave way to the term "traumatic neurosis of war," a disease in which the trauma was considered to be psychologic. With realization of the heavy burdens carried by the Government with respect to the care of neurotic veterans, medical efforts at the start of the present war were directed toward the screening of psychoneurotics and the early recognition and treatment of the symptoms of war neurosis. The medical literature is replete with contributions by neuropsychiatrists; much has been written on the subject of war neuroses — descriptive, statistical, interpretive and dynamic.[2-7] Most important in medicine, however, is a consideration of the etiology, pathology and therapy of this condition. It is the purpose of this paper to present some observations bearing on these problems.

First, it is necessary to define clearly what is meant by war neurosis and to clear up the terminology by which the topic is bound in the literature. The term "shell shock," already alluded to, proved to be a misnomer. Moreover, it is cogent to point out that the term "neurosis" is not fashionable in military circles because of its effect on the morale of the troops. Thus, the substitution of many different terms occurred, for example, "war fatigue," "exhaustion," "operational fatigue," "combat fatigue," "flying stress," "pilot fatigue," "war nerves," "war weariness" and "war jitters." It is obvious that one must rid oneself of this verbiage in order to define "war neurosis." One must confess that this term also is not particularly desirable, because this condition has little or nothing to do with the neuroses of civilian life.

The first criterion of the so-called "war neurosis" is the absence of a psychoneurotic history and the existence of an essentially stable personality with a satisfactory adaptation to life. Such is usually not the case in the neuroses encountered in civilian practice. Therefore, those persons with a psychoneurotic background who break down under the stresses of combat service, and quite logically are more prone to do so than the non-neurotic, are excluded from the group of patients with true war neuroses. The second criterion demands a combat experience of sufficient intensity to precipitate the neurosis. The immediate precipitating factors are of essential significance in this condition, in contrast to the deep-seated psychologic conflicts that are important in the true psychoneurosis unrelated to the war experience. Two other criteria must be satisfied to establish the diagnosis of war neurosis: an acute onset of irritability approximating a constant state of panic, and a relatively quick cure in the acute cases. Thus, war neurosis is a clinical entity characterized by the appearance in a previously stable person of nervous reactions precipitated by a severe catastrophic experience and amenable to quick recovery.

The characteristic symptom of this disorder is the repetitious catastrophic nightmare that has been described in observations of patients in the front lines. This consists of repeated re-enactments of the threatening combat experiences the patient has endured in cumulative fashion. As a result, sleep is disturbed and the patient is harassed by terrifying nightmares. Fear dominates the picture, even in the waking state and, with the increasing fatigue due to insomnia, produces the physical signs of tension and anxiety. The patient usually shows extreme restlessness, irregular tremors, exaggerated reflexes, excessive sweating and a frightened facies resembling the Parkinson attitude. Instead of the anxiety picture, some patients show a listless apathy reminiscent of the affectless schizophrenic.

The so-called "startle reaction" is the second characteristic of war neurosis. Sudden noises, by day or by night, produce in the patient a sudden start, accompanied by the physiologic manifestations of anxiety — tremor, dilated pupils, increased sweating, dry mouth, flushing or pallor and palpitation. No malingerer can successfully imitate this delicate timing of the physiologic effects of anxiety. Not infrequently the startle reaction breaks over into actual panic; the patient runs to the railing of the ship and attempts to jump overboard, screams hysterically or stands transfixed, laughing and crying uncontrollably.

Another sign germane to the clinical picture has been termed "a subtle personality change." The patients become morose, sullen, irritable and intolerant of their shipmates. They do not socialize in a normal way; they seek companionship in drinking; they show indecision and have inner feelings of unrest. It is not always easy to distinguish this personality change from that which accompanies a major psychoneurosis or psychosis. But it is

*Read at a meeting of the Baltimore City Medical Society, Baltimore, January 21, 1944.

†Neuropsychiatrist, United States Marine Hospital, Baltimore; assistant visiting neurologist, Boston City Hospital, assistant visiting neuropsychiatrist, Beth Israel Hospital, Boston, and assistant in neurology, Harvard Medical School (on leave of absence).

to be emphasized that this is not a cardinal sign of war neurosis, and the condition may exist without this phenomenon. There is still a fourth clinical manifestation, also not essential for the diagnosis, namely, a guilt reaction with emotional depression. This is manifest in many survivors of disasters in which a number of the original group were lost.[8]

With this description of the symptomatology of war neurosis, a few illustrative case histories will be presented.

## Case Reports

Case 1. C.B., a 44-year-old, married Coast Guard lieutenant, was admitted to the United States Marine Hospital in a state of severe anxiety characterized by insomnia, terrifying nightmares, tremulous speech with inarticulation and hypersensitivity to noises. He had been in the Navy since 1917 and had served the Coast Guard continuously for the past 20 years. He was on sea duty most of the time, and worked up from the ranks, becoming a senior lieutenant a year previously. He was always in good health, with a stable personality. For the last year and a half he had been on active duty in the South Pacific as chief engineer on a transport ship, working 16 to 20 hours a day in torrid heat, subjected to continual air raids and witnessing the death of his shipmates and even of officers sent to relieve him. During the past few months he had become physically exhausted and had shown signs of dehydration. He felt himself slipping until he could no longer control his nerves. He was unable to sleep, was disturbed by nightmares and was easily startled by the noises in the engine room. While standing watch he was overcome with fear and became tense and tremulous. He was irritable, morose and practically inarticulate, and was finally returned to the United States, arriving in a state of collapse.

When examined on admission a month later, the patient showed a rugged physique, coarse, generalized tremors and an expressionless facies. Speech was inarticulate. He was extremely tense and anxious and appeared to be confused. He realized that his mind was not working well, and he felt utterly hopeless about his future. He was oriented and showed no memory defects. He was still suffering from terrifying nightmares and fear of the slightest noises. This continued during the first part of his hospitalization and was punctuated by startle reactions to the sound of the practice air-raid sirens.

After 2 weeks of intensive treatment with large doses of bromides and chloral hydrate, the patient showed considerable improvement. Psychotherapy was given in the form of reassurance regarding recovery and free discussion of his combat experiences. Sedation was continued for the next 4 weeks in decreasing dosage. After 2 weeks of freedom from symptoms without medication, he was discharged home fully recovered and reported for active duty a month later.

Case 2. G.S., a 35-year-old merchant seaman who had been going to sea for 12 years, came to the hospital because of severe insomnia of 5 months' duration. He served in the Navy for 4 years and was honorably discharged in 1931. He was always in good health and never showed signs of nervous instability. Since the beginning of the present war he had sailed on tankers. About a year previous to admission his ship was torpedoed twice, and for the first time he became acutely aware of the dangers of the sea in wartime. During his last voyage he was on a freighter carrying a cargo of explosives and traveling without convoy or protecting planes. He began to have vomiting spells, frequency of urination, thumping of the heart and spasms of shaking and was startled by noises.

On examination the patient looked wan and drawn. He showed coarse tremors and hyperactive reflexes. He was tense and apprehensive and admitted that he had been disturbed by the constant threat of danger on the high seas. He talked incessantly about the ship's traveling alone without any protection whatsoever and carrying a dangerous cargo, exposing him to certain death in the event of a submarine attack. He suffered from nightmares of fierce torpedoing of his lone ship.

With heavy sedation continued for a week he improved and was transferred to the Maritime Service Rest Center for further care.

Case 3. M.A., a 21-year-old married merchant seaman, entered the Maritime Service Training School a year previously and had been going to sea for the last 5 months. He was the second youngest of six siblings and had an older brother who was also in the service and was injured on the same ship. He attended school up to the seventh grade and after training in a vocational school became a welder. He had had no previous illnesses.

During the last voyage, his ship was torpedoed and sunk, and he was rescued from a life raft by a destroyer and taken to North Africa. He was trembling with fear, was unable to sleep or eat and vomited continually throughout the trip. Whenever a depth charge went off, he became terrified and wanted to jump overboard. On arrival home a month later, he showed the typical symptoms of anxiety. His sleep was disturbed by terrifying nightmares, and his stomach was constantly upset.

On examination the patient showed generalized tremors, vasomotor instability and hyperactive reflexes. He found it difficult to talk, the words sticking in his mouth. He became emotionally unstable when he attempted to describe his terrifying experiences at sea. He admitted that he was more scared than sick, and he could not completely wipe out the memory of his experiences. He was put on sedation and was followed as an outpatient for a few weeks. He received tremendous solicitude from his wife and friends and finally had to be hospitalized on account of an increase in his symptoms.

With mild sedation in the hospital, followed by a period of rest in the Maritime Service Rest Center, the patient's symptoms largely subsided. He was extremely anxious to return to sea with his brother, who had recovered from his injuries.

Case 4. R.T., a 42-year-old merchant seaman who had been going to sea for several years, and whose ship was torpedoed in January, 1942, continued on duty throughout the following year. He was on a long voyage around Russia and had been blockaded in port there for 10 months. He suffered from inadequate and insufficient food and was greatly disturbed by the tremendously high prices that he had to pay for the necessities of life.

When the patient finally returned to the United States, he became tremulous and fearful and found that he was much dissatisfied with conditions here. He became sullen and morose and took to heavy drinking. He showed extreme hypersensitivity to the slightest noises and was particularly oppressed by practice air-raid sirens. He was unable to sleep and had nightmares picturing life in Russian ports.

On frequent interviews in the hospital, it was learned that the patient had been in rugged health and was extremely fond of seagoing life. He felt acutely the importance of sailing the ships to aid the total war effort. He had numerous complaints about the strategy of the American ships overseas, and could see no reason why he was required to remain completely idle in a Russian port for long periods of time. He showed no physical abnormalities other than general tremulousness and the startle reaction to the slightest noise. He showed considerable bitterness toward the Government for what he considered incompetency in the war plans.

With strong sedation he quieted down considerably, and he was given an opportunity to air his views about the factors of morale in the Merchant Service. After a few weeks he could no longer remain in the hospital and left to return to sea.

Case 5. G.B., a 23-year-old, married merchant seaman, was seen in the outpatient department in an anxiety state consisting of jittery feelings, sensations of tightness in the stomach, vague pains in the chest and confused thinking.

The patient attended high school and began to work in various factories at the age of 17, and later worked on fishing boats around New York. He joined the Maritime Service in January, 1943. On his first trip the ship was torpedoed and sunk, and he was rescued from a lifeboat by a destroyer, and after a few days was transferred to an American transport and brought home. He had difficulty in sleeping and experienced bad dreams about air-raid bombings and submarine attacks. For a month it was a struggle for him to decide whether or not to return to sea, but he finally decided to do so, since he did not wish to be accused of taking the easiest way out by being drafted. On his next trip in July, after being subjected to repeated bombings from the air, his symptoms increased. After the ship was torpedoed and

sunk, he was rescued and brought home as a passenger on another ship. He was terrified by seeing many of his shipmates killed and others removed to hospitals overseas. He had been home for the last 6 weeks, and had become increasingly worse. His wife noticed that he was extremely irritable and morose, and that he complained of numerous symptoms referable to his stomach. He was startled by the slightest noise and was unable to sleep on account of terrifying nightmares.

On examination the patient showed no physical abnormalities except for general tremulousness. He was mentally clear and talked rationally. He showed some anxiety about the risks of sea duty in wartime, but he felt ready to go back to sea on account of the vital importance of sailing the merchant ships in the war effort.

He was persuaded to go to the Maritime Service Rest Center, where he remained for a short time. He was then advised to take a shore job for a few weeks, and gradually improved, regaining his ability to sleep and losing his stomach symptoms.

As already mentioned, the immediate precipitating factors are of primary etiologic importance in war neurosis.[9] Nevertheless, a number of environmental factors, physical and mental, must be given consideration in the etiology. These include physical exertion, loss of sleep, insufficiency and irregularity of meals, continued exposure to bodily danger, loss of comrades in death, repeated near escapes from the enemy, frustration of necessary retreat and poor morale. It is not possible to evaluate the number and the severity of the factors necessary to produce a nervous breakdown in any given person, since there is great variability in the response of normal men to stresses. Those encountered in the type of case discussed here are peculiar to war conditions and are characteristically cumulative. It is significant that most of the patients do not break down after the first traumatizing experience, but usually after repeated exposure. This was true of the British experience in the evacuation of Dunkirk, when large numbers of men developed acute war neuroses.[10]

It is obvious that physical fatigue plays a large role in reducing the normal mechanisms of defense against emotional disturbance. Fatigue is important not only in land troops but also in men of the naval forces whose rest is usually broken by general alarms, drills, abortive attacks and the like. Fatigue has been such a prominent factor in the etiologic background of these cases that it has been suggested as an alternative term for the syndrome of war neurosis. Physical exhaustion, complicated by varying degrees of starvation, avitaminosis, dehydration and acidosis, is frequently met with.

Of more direct importance in the production of symptoms is the setting of interpersonal relations. In the war situation morale is a potent force in maintaining stability.[11] It is often found that the patient entered the combat situation without confidence in his leader. Any incident that strengthens faith in the leader lessens the occurrence of neurotic symptoms. Careful and adequate training is also of great importance in the prevention of war neurosis. It has been repeatedly observed that in the heat of battle men react at an automatic level and that fear reactions are much less frequent in those performing duties that they know well. Another factor often encountered is the intolerable sense of personal danger felt by a man surrounded by new shipmates whose conduct under fire he has not had time to estimate. He is consequently beset with feelings of doubt and insecurity, adding to the fear reaction.

Other psychologic factors, already referred to, likewise operate through the medium of fear. Prolonged exposure to bodily danger without relief has a tremendous effect on even the hardiest of personalities. Repeated near escapes from the enemy and the constant necessity of retreat produce a profound feeling of frustration. The subject is hence unable to discharge his aggression toward the enemy and, witnessing the death of his comrades about him, he becomes paralyzed with fear. These accumulated fear reactions give rise to anxiety and form the essential etiologic basis on which the immediate combat experience operates to precipitate the symptom complex called "war neurosis."

It is now in order to suggest the pathology of this condition by explaining the mechanisms of fear and anxiety in the organism. From the work of Cannon and his colleagues,[12] it is clear that the majority of the symptoms of fear and anxiety are related to the function of the sympathetic-adrenal apparatus. When such a state of sympathetic excitement is long continued, secondary effects result from the glycogenolysis, insomnia, anorexia and hyperventilation that accompany the prolonged adrenal activity. The emotion of fear is a perception in consciousness of these intense and complex somatic changes. In the light of Pavlov's conceptions, this emotion can be considered as a neurochemical reflex that is conditioned by environmental factors to reaction or inhibition by means of various summations, extinctions and facilitations. The fear reaction is a complex reflex, with its efferent arc proceeding through the sympathetic-adrenal innervation from the autonomic centers of the hypothalamus; these in turn are controlled from the cerebral hemispheres, whose function, in the words of Pavlov, is "that of reacting to signals presented by innumerable stimuli of interchangeable signification." Anxiety is an overaction of this fear reflex. By repetition and summation of the stimulus of danger, with constant reinforcement and lack of time for extinction, the reflex becomes either highly facilitated or conditioned to wider and wider associations, until the whole environment becomes an appropriate stimulus of fear. Moreover, analogous to the so-called "analyzer breakdown" of Pavlov's dogs, if the powers of adaptability to danger are overtaxed they may be entirely lost, the fear reaction being left disorganized and uncontrolled. Finally, interference with this mechanism by organic factors of fatigue or disease plays

a part in the cortical breakdown. It may be said, then, that in war neurosis occurring in the setting of continued combat without relief, a dissociation occurs between the cortical activity and the subcortical emotional and vegetative functions.

There are described in the literature other clinical pictures under the heading of war neuroses. They include severe exhaustion states; confusional states varying from mild disorientation to profound delirious reactions with hallucinations; dissociated states, such as amnesias, fugues and localized hysterical phenomena with various visceral disturbances; and acute psychotic and psychopathic disorders resembling the depressions, manic excitements and schizoid reactions. These represent a wide variety of neuropsychiatric conditions and are to be distinguished from the uncomplicated war neurosis. Those cases in which the patients develop complicating symptoms of all gradations of psychoneurosis, psychosis and organic brain disease should be grouped with the classic neuropsychiatric conditions common to civilian practice in which the combat situation is only an incident. In the cases presenting secondary signs, the treatment, prognosis and disposition are exactly the same as those for the same disability occurring in peacetime, except as they may be affected by the secondary gain possible under the pension system to any disability occurring during war. Unfortunately, this has proved to be an extremely serious obstacle in the handling of veterans of World War I.[12]

From the foregoing discussion, it may be seen that war neurosis is a clinical entity with specific diagnostic criteria and etiologic factors, having its pathologic basis in fear. The therapy of the condition is likewise specific. Foremost in importance is the principle of early treatment in the forward areas. The further away from the combat zone the patient is and the longer the treatment is delayed, the poorer is the prognosis. The latest Army figures show that 80 per cent of the patients treated without delay were returned to duty, whereas only 5 to 10 per cent of those evacuated to the rear were cured.

The active therapy is relatively simple and includes two primary considerations: rest and emotional desensitization of the patient to the traumatic combat experience. Rest is obtained by the use of barbiturates to produce profound and prolonged sleep. Supportive treatment with fluids and nourishment should be employed as indicated. Emotional desensitization may be accomplished by simple psychotherapy consisting of reassurance, exhortation, support and encouraging verbalization of the patient's fears. Hypnosis may be used, but deep analysis should be avoided. It is the precipitating factor of the combat situation that is basically significant in war neurosis, and not the unconscious conflicts such as exist in the true psychoneurotic. Group therapy has a place in dealing with large numbers of these casualties. Another technic of desensitization now in general use consists of allowing the patient to re-enact the frightening memories of his combat experience during narcosis produced by the intravenous administration of amytal sodium. This enables the patient to discharge the content of his fears and recover his amnesias, and to obtain reinforcement through suggestion and reassurance on the part of the physician.

Return to duty should be accomplished as soon as possible, but it is important that the patient be given a certain period of time to "digest" the emotional turmoil before being exposed to another. For this purpose he should have access to a center where directed recreation and physical work are available and simple psychotherapeutic methods are in use. He should be sleeping well, having no nightmares and exhibiting no startle reaction before he is allowed to leave. Those cases requiring further treatment are no longer useful to the service and come under the care of the Veterans Administration, when a well-rounded program of active psychiatric treatment and elimination of the complications incident to continuing disability benefits must be established. This is of vital importance in order to avoid repetition of the governmental burdens of the last war with respect to the care of veterans with neuropsychiatric disabilities.

## Summary

War neurosis is a clinical entity characterized by the appearance, in a previously stable person, of fairly constant nervous reactions precipitated by a severe catastrophic experience and usually amenable to quick recovery. The essential etiologic basis lies in accumulated fear reactions amounting to a state of anxiety under continued combat conditions without relief. The mechanism consists of overaction of the sympathetic-adrenal apparatus and the conditioned-reflex reactions of fear, as a result of which a dissociation occurs between cortical activity and subcortical emotional and vegetative functions.

## References

1. Neuropsychiatry. *The Medical Department of the United States Army in the World War*. Washington, D. C.: Government Printing Office, 1939.
2. *The Neuroses of War*. Edited by E. Miller. 250 pp. New York: MacMillan Company, 1940.
3. Gillespie, R. D. *Psychological Effects of War on Citizen and Soldier*. 251 pp. New York: W. W. Norton Company, Inc., 1942.
4. Maskin, M. Psychodynamic aspects of war neuroses. *Psychiatry* **4**:97, 1941.
5. Dunn, W. H. War neuroses. *Psychol. Bull.* **38**:497–504, 1941.
6. Kardiner, A. *The Traumatic Neuroses of War*. 258 pp. New York: Paul B. Hoeber, Inc., 1941.
7. Rado, S. Pathodynamics and treatment of traumatic war neurosis (traumatophobia). *Psychosomatic Med.* **4**:362–368, 1942.
8. Kubie, L. S. Manual of emergency treatment for acute war neuroses. *War Medicine* **4**:582–598, 1943.
9. Goldstein, K. On so-called war neuroses. *Psychosomatic Med.* **5**: 376–383, 1943.
10. Sargant, W., and Slater, E. Acute war neuroses. *Lancet* **2**:1, 1940.
11. Raines, G. N. and Kolb, L. C. Combat fatigue and war neurosis. *U. S. Nav. M. Bull.* **41**:923, 1943.
12. Cannon, W. Cited by Best, C. H., and Taylor, N. B. *The Physiological Basis of Medical Practice*, 1942 pp. Baltimore: Williams & Wilkins Company, 1943.
13. Aring, C. D., and Bateman, J. F. Nurturing a national neurosis. *J.A.M.A.* **109**:1092–1096, 1937.

## CLINICAL NOTE

# SPONTANEOUS PNEUMOPERITONEUM FROM AN UNKNOWN CAUSE*

### Report of a Case

Nathan Sidel, M.D.,† and
Abraham Wolbarsht, M.D.‡

Boston

PNEUMOPERITONEUM may be a spontaneous, diagnostic or therapeutic condition. When it is encountered, except in the form induced for diagnosis, there is usually some lesion in the gastrointestinal canal as the causative factor. The perforation of a viscus is the usual cause, and in some cases the perforation is a slowly developing leak rather than a sudden puncture.

This case report deals with a rarely reported finding, spontaneous pneumoperitoneum without demonstrable cause and without symptoms. According to Hinkel§, the case he reported was the third such report in a review of the literature, and none has been reported since.

### Case Report

I. N., a 63-year-old Swede, was admitted to the First Medical Service of the Boston City Hospital on May 7, 1940. There was a 2 weeks' history of an upper respiratory infection followed, 2 days before admission, by a frank chill and pain in the left side of the chest, aggravated by coughing and breathing. The past history and family history were not remarkable.

Physical examination revealed a well-developed and well-nourished male, moderately ill and breathing somewhat laboriously. Except for a reducible right inguinal hernia, the positive physical findings were limited to the chest. There was limited expansion of the left chest, with increased tactile fremitus, dullness, an increased whispered voice and a few medium moist rales at the left base. The temperature was 100°F., the pulse 96, and the respirations 26. A diagnosis of pneumonia of the left lower lobe was made and the patient was started on routine pneumonia care and sulfapyridine. Both the sputum and the admission blood culture were reported as positive for Type 8 pneumococcus. Subsequent blood cultures were negative. X-ray examination of the chest the day after admission also indicated pneumonia of the left lower lobe. The patient became afebrile on the 2nd day and remained so the entire 1st week, except for a rise in temperature to 100°F. on the 2nd day. The sulfapyridine was discontinued on the 3rd day.

On the 5th day, slight abdominal distention was noted, and a few medium moist rales were heard at the base of both

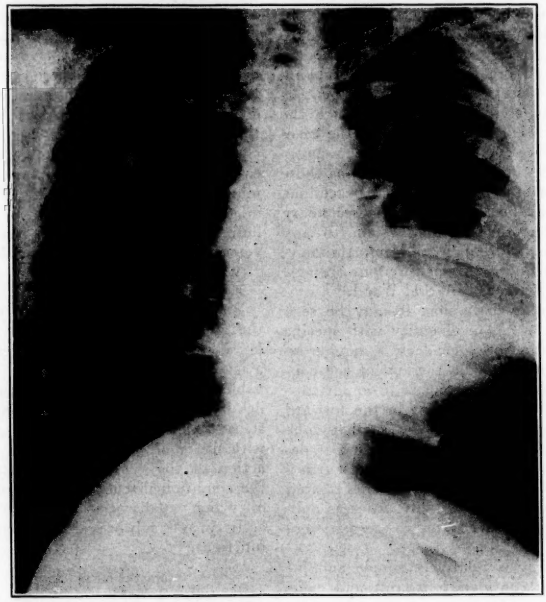

Figure 1. *Roentgenogram Taken on June 3.*

*From the First Medical Service, Boston City Hospital.

†Assistant professor of medicine, Tufts College Medical School; assistant visiting physician, Boston City Hospital; associate visiting physician, Beth Israel Hospital.

‡Formerly, intern, First Medical Service, Boston City Hospital.

§Hinkel, C. L. Spontaneous pneumoperitoneum without demonstrable visceral perforation. *Am. J. Roentgenol.* 43:377-382, 1940.

lung fields. The distention became progressive and firm. The patient had no complaints except for general discomfort due to the distention. He was given enemas, flaxseed poultices and pituitary extract and rectal tubes were passed, with little reduction in the distention which continued unabated for slightly more than 3 weeks, when it began to decrease progressively. In the 3rd week, because of a continued daily slight rise in temperature and persistence of rales at both bases, another course of sulfapyridine was started and continued for 5 days. The patient again became afebrile for over a week. This was followed by a few days of elevated temperature. From the middle of the 5th week until discharge in the 6th week, he remained afebrile and asymptomatic.

X-ray examination of the chest on the 17th day showed diffuse clouding at the lower half of the left lung field and also a concave shadow at the right base, which was interpreted as being suggestive of a large amount of free air beneath the diaphragm. A flat plate of the abdomen taken on June 3 showed an extensive pneumoperitoneum with the liver and spleen outlined (Fig. 1). The abdominal organs shifted with change in position. Fluoroscopy showed normal movements of both sides of the diaphragm. A barium meal passed normally through the esophagus and entered the stomach without delay. There was no evidence of gastric or duodenal ulcer.

After complete recovery from the pneumonic process and reduction in distention, a gastrointestinal series was performed, which was interpreted as showing hypertrophic gastritis. Lipiodol was injected into the lungs to discover whether a fistula into the peritoneum had occurred through the diaphragm. The results were entirely within normal limits except for slightly thickened pleura on the left. A barium enema was negative. At that time (July 5) the x-ray examination still showed air under the diaphragm.

On July 27 a fluoroscopy of the abdomen demonstrated complete absence of air in the peritoneum. X-ray examination on August 10 (Fig. 2) showed complete disappearance of the pneumoperitoneum.

A review of the past history failed to reveal any abnormal gastrointestinal background. There were at no time complaints referable to the gastrointestinal tract, either during the hospital stay or subsequent to discharge.

Laboratory studies during the hospital stay were not remarkable except for one urine specimen containing sulfapyridine crystals. The stools were negative for occult blood on several occasions. The hemoglobin ranged between 78 and 84 per cent (Sahli) and the white-cell count varied between 7500 and 12,000. The blood smear differentials were normal. A blood Hinton test was negative. The blood nonprotein nitrogen on two occasions was 40 and 59 mg. per 100 cc.

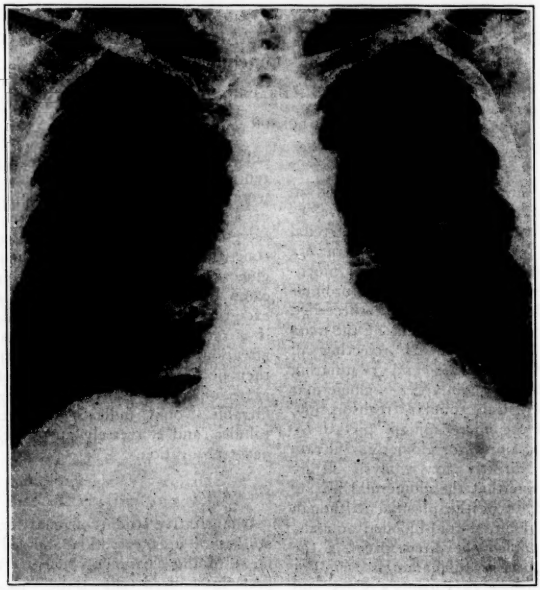

FIGURE 2. *Roentgenogram Taken on August 10.*

It is generally recognized that the demonstration of pneumoperitoneum, except for the form induced for diagnostic purposes, is indicative of a perforated viscus due to a peptic, typhoidal, tuberculous or carcinomatous ulcer in the stomach or intestine or to serious abdominal trauma.

Occasionally, pneumoperitoneum is not demonstrable even though a definite perforation in the gastrointestinal tract has taken place as shown at operation or autopsy. When pneumoperitoneum is present, however, one can generally assume that perforation has taken place. Cases are reported of recovery from perforation without surgical intervention and the subsequent disappearance of the pneumoperitoneum, but in these cases a gastro-

intestinal lesion is diagnosed either by x-ray evidence or from the history. In this case, no history or x-ray findings of a gastrointestinal abnormality were obtained, and the patient remained essentially free of abdominal symptoms.

SUMMARY

A case of pneumoperitoneum discovered accidentally during the course of pneumonia without any symptoms referable to the pneumoperitoneum is reported. There was a subsequent spontaneous disappearance of the pneumoperitoneum. This case is considered unusual because no gastrointestinal abnormality was shown by the history, laboratory tests or x-ray investigation. There was x-ray evidence of the marked pneumoperitoneum and the complete disappearance of such findings after a three-month interval.

The possible relation of a pneumoperitoneum to the pneumonic process by the formation of a fistula was investigated, but no basis for it was discovered.

## MEDICAL PROGRESS

# MODERN CONCEPTS OF RENAL STRUCTURE AND FUNCTION IN CHRONIC BRIGHT'S DISEASE (Concluded)*

STANLEY E. BRADLEY, M.D.†

BOSTON

### FUNCTION

During the past year Smith[42, 43] has published an engaging and intimate account of the development of the modern concepts and methods of renal physiology. As he points out, the modern era began with the appearance of Cushny's[44] monograph, *The Secretion of Urine*, and the promulgation of his "modern view." Cushny succeeded in establishing order and coherence among the mass of data that had accumulated by rejecting all of the many existing theories and postulating but two renal excretory activities — glomerular filtration and differential tubular reabsorption. The introduction of the microcapillary pipette by Richards[45] to obtain samples of glomerular filtrate and tubular urine directly for analysis firmly established the doctrine that the glomerular filtrate is a simple ultrafiltrate of the plasma. Although the early work was done on cold-blooded animals, recent work has extended the direct proof of the validity of this hypothesis to mammals.[46, 47] For many years the influence of Cushny's ideas and the absence of solid evidence excluded the possibility of tubular excretion, but in 1923, Marshall and Vickers[48] showed that phenol red was excreted by the kidney even when the perfusing pressure was too low to permit filtration. Moreover, they noted that more phenol red appeared in the urine of the normal animal than could possibly be excreted by filtration alone since most of the dye is bound to the plasma protein leaving only a small fraction available for filtration. Therefore, it seemed reasonable to conclude that a process of active tubular excretion must be concerned in the renal elimination of phenol red. To this evidence were added supportive data derived from a study of aglomerular fish.[35] In these animals urine is secreted in the absence of a filter bed and all the constituents that may be found in urine, save protein, glucose and ferricyanide, are voided. It soon became evident that quantitative study of tubular excretion and reabsorption could be possible only if a means of measuring the rate of glomerular filtration could be devised. Filtration rate could then be used as a standard of reference, since the excretion of any substance in excess of the amount filtrable would indicate a contribution by the tubules, and conversely any deficit would indicate net reabsorption.

#### *Clearances*

Quantitative studies of renal function began with studies of urea excretion and led to the development of the clearance concept. When Van Slyke first introduced the term "clearance" he had reference to the virtual volume of blood completely cleared of urea in each minute by the kidney, but as Smith[42] points out, the term has acquired broader meaning in recent years and "taking conceptual wings, has become a generalized notion applicable to all aspects of renal excretion." The first concept of the urea clearance was confused by the introduction of a square-root radicle into the term at low urine flows, "a mathematician's device to squeeze a correlation out of data in which a simple correlation is not present."[42] Once it was appreciated that the use of the square-root radicle had no physiologic justification, the situation was simplified: the clearance term could be applied to any substance, and the ratio between the quantity of the material

*From the Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

†Instructor, Department of Medicine, Boston University School of Medicine; assistant physician, Evans Memorial, Massachusetts Memorial Hospitals.

excreted each minute and its concentration in plasma or blood could be expressed in terms of a volume of plasma or blood cleared of it per minute. If a substance is to be used in measuring filtration rate it must be excreted only by filtration. The quantity cleared is the amount contained in the plasma that passes through the filter; its plasma clearance is equal to the filtration rate. In a phlorizinized animal, glucose is no longer reabsorbed and since there is no tubular excretion of this substance, it follows that, in this situation, the glucose clearance must be equal to the filtration rate. It has been found that glucose clearance in the phlorizinized animal is equal to the clearance of inulin, mannitol, sorbitol or dulcitol when these determinations are made simultaneously.[42] In the normal animal and in man, the clearance of glucose is zero, whereas the values for the other substances are identical with those in the phlorizinized animal. Hence there is good evidence that these substances can be used to measure filtration rate.

If all the blood passing through the kidney is completely cleared of a given substance, then the measurement of this clearance is equivalent to the measurement of blood flow. Among substances found to be approximately so cleared are Diodrast and sodium para-amino hippurate. Of course, one would not expect absolutely all the blood flowing through the kidney to be cleared, since a portion of it perfuses nonexcretory tissue. Nevertheless, recent determinations of the renal extraction ratio of sodium para-amino hippurate reveal that 90 per cent of the material, on the average, is removed on one circulation through the kidney.[41, 49] Therefore it seems fair to assume that the clearance of this material (and of Diodrast) is a measurement of the blood perfusing functional excretory tissue, that is, of *effective* renal blood flow.

With such methods for measuring glomerular filtration rate and renal blood flow, students of renal physiology and disease have been able to move on to quantitative studies of renal hemodynamics and tubular activity. For example, the ratio between filtration rate (GF) and blood flow (PF), namely, the filtrate fraction (GF/PF), is the percentage of the renal blood flow filtered at the glomerulus. This value is a function of a number of variables, including intraglomerular pressure, plasma oncotic pressure, intrarenal pressure and the viscosity of the blood. Smith and his associates[50] have undertaken an analysis of these variables with the aim of ascertaining the relative effect of vasomotor activity in the afferent and efferent glomerular arterioles. They showed that similar changes in all values result from *afferent* arteriolar control of blood flow, that is, a fall in GF, PF and filtrate fraction during increased afferent resistance, and a rise in all with decreased afferent resistance, whereas a constant filtration rate is maintained over a wide range of renal blood flows by *efferent* arteriolar control of intraglomerular pressure. Since the filtration rate tends to remain constant in normal animals and man, and also in hypertensive patients with a wide range of decreased renal blood flows, they concluded that the prime determinant of glomerular dynamics is *efferent* vasomotor activity. Lamport,[51, 52] however, in a subsequent analysis of the same data took issue with this conclusion. On the basis of formulations of afferent and efferent arteriolar resistances derived from Poiseuille's law, he deduced that both sets of arterioles must be active to maintain a constant filtration rate since, contrary to Smith's hypothesis, his calculations showed that *efferent* control would be expected to change filtration rate from zero at low blood flows to a maximum at normal flows and back to zero at high rates of renal blood flow, an obviously impossible physiologic situation. Shannon,[53] on the other hand, criticizes both hypotheses for their dependence on assumed constant values for immeasurable variables and points out that Lamport's treatment does not recognize the importance of the elastic resistance of the glomerular capillaries. Lamport[54] admits the justification of the first criticism, but claims that his calculations are flexible enough to account for all conceivable factors. The fundamental difference between these two hypotheses can best be seen when they are applied to an interpretation of the hemodynamic events of essential hypertension. Early in the course of this disease, the filtrate fraction increases as a result of the diminished blood flow through the kidney without significant change in the filtration rate. Smith[50] places the site of the vasoconstriction responsible for the decreased blood flow in the efferent arteriole, whereas Lamport[55] believes that the resistance in both arterioles is increased with afferent outweighing efferent vasoconstriction. Undoubtedly further analysis will resolve the differences between these two points of view.

The application of the clearance methods to the measurement of the dynamic activities of diseased kidneys has been severely criticized because of the over-all character of clearance measurements.[56] Thus the demonstration of hypertrophy and atrophy in the same kidney implies a compensation on the part of some units for the decreased function in others, allowing the average function of the two categories measured by clearances, to remain unchanged in spite of the marked local alterations that have occurred. This type of behavior has been demonstrated functionally, as well as anatomically, in dogs with chronic interstitial nephritis. These animals have been shown to handle a dye, trypan blue, in a manner different qualitatively and quantitatively from the normal since it appears that filtration with or without reabsorption and actual diffusion into the tubular lumen may take place. It is asked, then, Why may there not be a similar change in the manner in which inulin is excreted,

making it unsuitable as a measure of the filtration rate? Furthermore it has been shown that renal tubules severely damaged by uranium cease to excrete Diodrast and they allow inulin to diffuse back into the blood.[57] These criticisms appear to have been answered satisfactorily.[58] It is admitted that the clearances are average figures but, that, considered in relation to the total mass of active tubular tissue, they continue to have significance in assessing the relative changes in filtration rate and renal blood flow. Furthermore it has been demonstrated that the clearances of inulin and mannitol in glomerulonephritis,[59] eclampsia[60] and the profound renal hemodynamic changes of shock[61] are in agreement. If molecular diffusion in either direction between the tubular lumen and the blood occurred, then agreement of these values could not be expected, since the rates of diffusion would not be equal for such dissimilar molecules. It is immaterial for the measurement of blood flow how Diodrast or para-amino hippurate is excreted, provided the blood is entirely cleared. In renal disease, blood perfuses a smaller and smaller mass of excretory, relative to nonexcretory, tissue and as a result, the over-all extraction ratio would be expected to decrease. Obviously, with extreme damage the Diodrast (or hippurate ) clearance fails to measure even approximately the actual renal blood flow. As a matter of fact, extraction ratios as low as 55 per cent have been observed in a case of chronic diffuse glomerulonephritis in the nephrotic stage when over-all renal function was not greatly impaired.[49] This does not mean, however, that in such cases these clearance methods should be discarded as valueless. They continue to measure the blood flowing to residual functional excretory tissue, since it is unlikely that at the low plasma levels of Diodrast (or hippurate) employed the capacity of any perfused functioning tissue is exceeded. This surmise is strengthened by the demonstration that the proportionality between the amount removed by and the amount offered to the kidney at progressively higher plasma levels remains unchanged and normal in pattern until very late in the course of glomerulonephritis.[59] This indicates that the functional tissue is handling the substance in a normal fashion and that the Diodrast (or hippurate) clearance, in these circumstances, is a valid measure of blood flow to such functional tissue.

*Tubular Function*

The necessity of relating the renal blood flow to the mass of functional tissue became obvious when the problems of ischemia and hyperemia, of hyperfiltration and hypofiltration in residual glomeruli and of hyperfunction and hypofunction in variously damaged tubules were considered. To understand the methods used for assaying the mass of renal functional tissue one must return to the question of tubular reabsorption and excretion. Given a method for determining glomerular filtration, the role played by the tubules in the renal secretion of a given substance can be accurately quantitated; for example, at high plasma levels of glucose the amount of tubular reabsorption of glucose is equal to the amount filtered less the amount that appears in the bladder urine. Early in the study of tubular function it became apparent that many substances, particularly nonelectrolytes, were handled by tubular transfer mechanisms of definitely limited capabilities. For example, glucose is entirely reabsorbed from the glomerular filtrate until the load exceeds the capacity for reabsorption, when reabsorption continues at a fixed maximal rate while the excess is spilled in the urine. Similarly the excretion of Diodrast is limited by the maximal capacity of the tubules to handle it. Such maximal rates of either reabsorption or excretion are functions of the quantity of active tubular tissue. After unilateral nephrectomy the maximal rates are approximately halved,[24] and with the succeeding hypertrophy of the remaining kidney they slowly increase. Moreover, it has been shown that a clear-cut correlation obtains between glomerular filtration rate and maximal tubular activity (Tm) and that a similar relation holds for blood flow and Tm.[62] The wide variability of the discrete functions in persons of varying size vanishes when the clearance values are expressed in terms of these factors. Hence, in disease where all functions may be depressed, a knowledge of the *effective* renal blood flow of itself may be of no value in estimating the presence of renal ischemia or hyperemia, but when related to the mass of residual functioning tissue, it may give helpful information regarding these matters.

Saturation methods, such as those used in the determination of transfer maxima, have been applied to an analysis of the distribution of glomerular and renal vascular dysfunction[43, 63] and have, under certain circumstances, indicated the presence of coexistent hyperfunction and hypofunction. Shannon and his associates[64] have shown in the normal dog that glycosuria occurs abruptly and that all the nephrons apparently are simultaneously saturated (glucose Tm is reached) at a given level of plasma glucose. This requires a nice adjustment between the individual glomerular filtration rates and the capacity of the attached tubules to reabsorb glucose and implies an anatomic and physiologic correlation between the size of the glomerulus and its attached tubule such that the large glomeruli are attached to large tubules and small glomeruli to small tubules. If this adjustment did not obtain, glucose would begin to appear in the urine at plasma levels of glucose lower than those required to saturate all the nephrons, because at such low levels the maximal rate of reabsorption would be reached in tubules getting a larger proportional quantity of filtrate. Almost the same situation has been

found in man for both glucose and Diodrast.[63] With respect to the latter, the phenomenon indicates a proportional distribution of blood flow to every tubular excretory cell. Owing to this fact, a progressive elevation of the plasma level (so-called "titration" of the kidney) of either Diodrast or glucose is associated with an equal increase in the amount transferred by the tubular cells until Tm levels are reached, when the transfer rate abruptly becomes constant. This proportionality between the load and the transfer rate may be disturbed by disease. Hyperemia of some of the nephrons results in relatively higher perfusion and filtration rates allowing saturation of these units at low loads; whereas ischemia has a reverse effect. Mathematical and statistical analyses of the defects in proportionality have been published in the past year, and distribution curves for relative glomerular activity and tubular perfusion have been derived for normal kidneys.[63] These methods have also found application in the study of the kidney of essential hypertension.

Before turning to the application of these methods to the study of renal physiology in chronic Bright's disease, certain aspects of recent studies of tubular function must be considered with special reference to their bearing on renal disease. The discovery of maximal transfer capacity permits examination of the intracellular mechanisms by which these tubular activities are carried out. Thus, the effect of the presence of other substances that may interfere with enzymatic activity or that may enter into the reactions by which transfer is accomplished can be studied and inferences may be drawn concerning the nature of various intracellular metabolic processes. This is an extremely important consideration, since renal hypertension and other effects of renal dysfunction may arise from a derangement of intracellular activities of the tubular cells.[63] Shannon,[65] in an important review of this subject, has shown that the available data are consistent with an explanation of the phenomena of limited transfer in terms of the mass-action law, assuming the intermediacy of a transfer substance. During the past year, Pitts[66, 67] has reported the results of a study of the reabsorption of various amino acids and suggests certain modifications of Shannon's hypothesis, which are necessary to explain the kinetics of amino acid transfer. It is interesting that several substances appear to compete for excretion or reabsorption by the same mechanism. Several different series of such substances have been studied. Glucose, xylose, galactose and sucrose are apparently reabsorbed through the agency of one transport system,[63, 68] whereas phenol red, Diodrast, Hippuran,[69] Iopax, Neoiopax, Skiodan,[70] para-aminohippuric acid[71] and penicillin[72, 73] are excreted by another mechanism. In the case of the first system, preferential treatment is given to glucose, which, when present in sufficiently large amounts, excludes other members of the group from transfer. In the second series, Diodrast appears to be preferentially excreted and glycine heads a series of amino acids, including alanine, glutamic acid and arginine,[67] that are reabsorbed preferentially in the order named. The action of phlorizin has been interpreted by some workers as an effect of competition with glucose for an intracellular transport system,[53] although there is evidence that it produces its effect by interference with the action of kidney phosphorylase.[74]

Many tubular activities, such as water reabsorption and sodium or potassium transport, are known to be under endocrine control. It has recently been demonstrated that the hypophysis, adrenal cortex, gonads and thyroid gland are capable of affecting tubular transport systems. Hypophysectomy is followed by a decrease in Diodrast Tm and by a failure of hypertrophy to occur in the remaining kidney after unilateral nephrectomy.[75, 76] The administration of thyroid causes increased Diodrast transfer in animals.[77] Estradiol depresses the absorption of ascorbic acid[78] and causes renal hypertrophy, possibly on the basis of interstitial edema.[79] Testosterone administration is followed by hypertrophy of both kidneys in experimental animals[79–82] and an augmentation of Diodrast Tm.[83] For this reason it has been suggested that the trophic effect of testosterone might prove of value in stimulating hypertrophy of residual renal tissue in the course of Bright's disease.[81, 84] Furthermore, it was thought, that the retention of nitrogen due to increased protein building supposedly induced by testosterone administration, might serve a useful purpose in patients with nephrosis losing large amounts of protein.[85] Two cases of renal disease have been reported in which therapy was based on this rationale.[82, 85] There is no evidence of benefit. In Cushing's syndrome due to adrenocortical tumor, no change in Diodrast Tm or Diodrast or inulin clearance was noted by Barnett and his coworkers.[86] Moreover, Heinbecker and his group[77] failed to find any renal change following the administration of cortical extract to dogs, and desoxycorticosterone, in the hands of Winkler and his colleagues,[87] failed to produce any noticeable effect during anuria. The experiments of Selye and his co-workers,[88–93] however, revealed a profound change in the kidneys of experimental animals following the administration of desoxycorticosterone. These investigators discovered that this substance produced renal lesions in the chick resembling in every way nephrosclerosis,[92] but it was also found that excess salt ingestion produced similar lesions.[93] An extension of the study to mammals (dog, rat and monkey) disclosed that desoxycorticosterone overdosage combined with the ingestion of large amounts of sodium chloride produced renal lesions similar to those of malignant nephrosclerosis in man.[88, 89] Accompanying the development of the renal lesions

the blood pressure rose to hypertensive levels and death occurred on the basis of renal insufficiency and cardiac failure. Vascular lesions were found not only in the kidney but also in the pancreas and in the adrenal capsule. Recently it has been found that the action of desoxycorticosterone in the experimental animal may be completely blocked by methyl-testosterone.[94] What bearing these discoveries may have on the question of the etiology and therapy of human malignant nephrosclerosis remains to be seen.

Despite the sensitivity of tubular activities to many extrarenal influences, values of Tm in normal animals and man are strikingly constant and reproducible.[63] The maximal tubular transport rates of glucose and Diodrast have been shown to be constant and independent under a variety of experimental conditions. The administration of adrenalin and caffeine and the induction of renal hyperemia during pyrogenic reactions do not affect the values of glucose and Diodrast Tm to any significant degree.

The constancy of glucose Tm has important theoretical consequences. It has long been known that only a portion of the glomeruli are active at any one time in the amphibian kidney, and it has been supposed, on the basis of injection studies,[95] that a similar inactivity of an appreciable number of glomeruli may occur in the mammalian kidney. It has been assumed that caffeine diuresis in man follows induced activity of previously inactive glomeruli, which direct observation has shown to be the case in the frog. If this were true, a marked increase in filtration rate and in glucose Tm would be expected after the administration of caffeine because the opening up of nonfunctioning glomeruli would bring into operation nephrons previously not filtering and reabsorbing glucose, thus causing an increase in maximal reabsorptive capacity. This does not happen. On the other hand, adrenalin might be expected to shut down a number of glomeruli and to reduce Tm. Forster[96] has shown that this is the case in the frog, where glomerular intermittency can be directly observed, but no change in Tm occurs in man.[63] Hence, the facts "controvert the idea, carried into mammalian physiology from observations on cold-blooded animals, that any significant number of glomeruli are inactive at any moment."[63] In addition, direct observation of mammalian glomeruli has failed to reveal any evidence of glomerular intermittency.[47] Explanations of drug action in man based on this hypothesis must be discarded. Obviously the concept of a glomerular reserve is unfounded and the filtration rate may be taken as a measure of the filter bed.

*Functional Patterns of Disease*

Renal function in 22 patients in various stages of glomerulonephritis has been studied by the methods outlined above at the Welfare Island Hospital in New York City by Earle, Taggart and Shannon.[59] The earliest manifestation of the disease was an interference with the glomerular filtration rate, as one would expect on the basis of what is known of the pathology. In addition to the fall in filtration rate, renal blood flow increased or it remained at a normal level. As a result, the filtration fraction decreased from a normal level of 19 per cent to as low as 8 per cent. It is known that afferent vasoconstriction may lower intraglomerular pressure, with a fall in filtration rate and filtrate fraction. This appears to be the case in shock[61, 97] and in chronic anemia,[98] both of which are accompanied by a decreased renal blood flow. Since in glomerulonephritis, however, the blood flow may actually increase, it appears likely that the decreased filtration rate and filtration fraction found in glomerulonephritis are attributable to impairment of filtration caused by the action of the disease on the glomerular membrane.

At first there seemed to be relatively little interference with tubular function, and it was pointed out that the resultant loss of the normal adjustment between glomerular filtration rate and the functional capacity of the attached tubule may have serious consequences, since "glomerular damage out of proportion to the impairment of tubular function should predispose to the retention of electrolyte and, incidentally, water, as is so common."[59] With progression there was a destruction of tubular tissue roughly parallel to the reduction in filtration rate, as evidenced by the fall in the Diodrast Tm. Here too, however, there was relatively greater reduction in filtration rate than in tubular mass so that the glomerular filtrate-Diodrast Tm ratio (GF/Tm) remained depressed and glomerulotubular imbalance continued to be prominent. At first blood flow was well maintained, but when the Tm was reduced to half normal, the blood flow was consistently reduced to extremely low levels. It should be noted that high blood flow-Diodrast Tm ratios (PF/Tm), denoting relative hyperemia, were not uncommon in any phase of the disease.

The low filtrate fraction remained prominent during the entire course until the appearance of hypertension or the extreme reduction of Tm in the terminal stage either considerably altered glomerular dynamics or so invalidated the measurement of blood flow that the filtrate fraction rose to normal or high levels. At that time too, there was often a reversal in the glomerular filtrate-Diodrast Tm ratio (GF/Tm). Hypertension was not necessarily related to the extent of tubular damage, although it seemed to be consistently present when Tm had been reduced to one quarter normal. During the acute stage and in acute exacerbations of the chronic disease a reduction was observed in filtration rate, Diodrast Tm, and GF/Tm, followed by a return toward the normal levels during recovery, but no

correlation was apparent between the gravity of these changes and the ultimate course of the disease. Occasionally the values returned to normal while proteinuria was still obvious. Two findings stand out in this study, namely, the predominance of glomerular impairment and the appearance of relative renal hyperemia throughout the course of the disease. These features are consistent with the pathology and with the belief that glomerulonephritis is pre-eminently an inflammatory disease.

The functional pattern of glomerulonephritis stands in striking contrast to that found in the course of nephrosclerosis. Sixty subjects with essential hypertension were examined by Goldring, Chasis, Ranges and Smith.[99] Early in the disease changes in filtration rate and renal blood flow appeared to be based upon hemodynamic rather than upon organic changes. The filtration fraction was increased as a result of decreased blood flow in the presence of an unchanged filtration rate. The authors are of the opinion that this pattern is caused by efferent arteriolar vasoconstriction that is functionally reversible (hyperemia followed the administration of pyrogenic inulin with a fall in the filtration fraction) and that it is not dependent on neural pathways (the pattern remained unchanged after extensive sympathectomy) and is therefore probably attributable to the activity of some unknown humoral agent. With progression of the disease there was a steady loss of tubular tissue manifest in the gradual reduction in Diodrast Tm, a loss that at times outran the impairment of filtration, thus indicating the presence of impotent tubules or possibly increased pressure in the glomerulus as a result of increased systemic arterial pressure. Whereas the glomerular filtrate-Diodrast Tm ratio (GF/Tm) tended to increase, unlike the situation in glomerulonephritis, the renal blood flow-tubular excretory mass ratio (PF/Tm) ranged from low normal to very low values, thus indicating relative renal ischemia. A study of the distribution of blood to its tissue substrate during hypertensive disease, however, revealed fairly uniform spread even when the disease was so far advanced as to distort markedly the anatomy and the delivery of filtrate.[63] Focal renal ischemia appeared to be the exception rather than the rule in this disease. The slight increase in Diodrast Tm that often followed the administration of pyrogen might have been evidence that in some cases highly ischemic tubules were brought into perfusion by hyperemia. The distribution of glomerular filtrate to tubular reabsorptive mass (glucose Tm), on the other hand, showed a marked distortion with a tendency for the over-all filtration rate to remain within normal limits, owing to the opposing operation of large numbers of hyperemic and ischemic glomeruli. It is interesting that the earliest, most persistent and most consistent finding in the hypertensive kidney was a reduction in Diodrast Tm, usually considerably in excess of the glucose Tm. This finding indicates that two activities presumably localized in approximately the same segment of the nephron may be affected differently by the same disease process. Glucose Tm fell only after a considerable change in Diodrast Tm had occurred, and it was thought that this preferential depression of the rate of Diodrast excretion might arise out of an interference by the disease with intracellular metabolic activities and indeed might point to the primary defect in the kidney in essential hypertension.[63] In summary, the renal functional picture during the course of essential hypertension seems to be one in which the progressive reduction in Diodrast Tm is associated with a reduction in renal blood flow, little or no change in filtration rate and an elevation in the filtrate fraction, all of which are probably attributable to the hemodynamic factor of increased arteriolar tone (predominantly efferent). There is little alteration in the distribution of blood to each unit of the parenchyma, but a marked distortion in the distribution of filtrate to the tubules, probably again on a hemodynamic basis, so that hyperfiltration in some units balances hypofiltration in others and maintains an over-all filtration rate within normal limits.

Renal functional patterns have not yet been clearly defined in the nephroses. A number of the patients studied by Earle and his co-workers[59] were examined during the nephrotic stage of glomerulonephritis. There were no distinctive features by which these patients could be distinguished from others suffering from chronic diffuse glomerulonephritis. In nephrotic children, however, it has been known for several years that the urea clearance is increased.[100] The inulin clearance has been found to be elevated as much or more than the urea clearance,[101] and during the last year Emerson and Dole[102] reported increases in both inulin and Diodrast clearances with a slight elevation of the filtration fraction. They attribute the supernormal urea clearance to increased renal blood flow.

* * *

Obviously a considerable amount of work remains to be done. Knowledge of functional patterns during chronic Bright's disease is faulty and incomplete. Although many new methods have been developed by which quantitative studies of renal activities may be made, they have found intensive use only in the study of glomerulonephritis and of essential hypertension. Pyelonephritis and the various nephroses await similar investigation. These studies are of the greatest importance from the standpoint of pathogenesis, diagnosis, prognosis and treatment. The discovery that certain functional hallmarks distinguish glomerulonephritis and essential hypertension may find use in differential diagnosis. Further special investigations may reveal facts on which prognostic criteria can be safely established. Elucidation of the etiology of chronic Bright's disease, clarification of the difficult prob-

lems of hypertension and improvement of therapy may result from an intensive examination of tubular intracellular metabolic activity.

65 East Newton Street

## References


42. Smith, H. W. William Henry Welch Lecture. I. Renal physiology between two wars. *J. Mt. Sinai Hosp.* **10**:41-58, 1943.
43. *Idem. Lectures on the Kidney.* 134 pp. Lawrence, Kansas: University of Kansas, 1943.
44. Cushny, A. R. *The Secretion of the Urine.* 241 pp. London: Longmans, Green & Co., 1917.
45. Richards, A. N. Physiology of kidney. *Bull. New York Acad. Med.* **14**:5-20, 1938.
46. Walker, A. M., and Oliver, J. Methods for collection of fluid from single glomeruli and tubules of mammalian kidney. *Am. J. Physiol.* **134**:562-579, 1941.
47. Walker, A. M., Bott, P. A., Oliver, J., and MacDowell, M. C. Collection and analysis of fluid from single nephrons of mammalian kidney. *Am. J. Physiol.* **134**:580-595, 1941.
48. Marshall, E. K., Jr., and Vickers, J. L. Mechanism of elimination of phenolsulphonephthalein by kidney proof of secretion by convoluted tubules. *Bull. Johns Hopkins Hosp.* **34**:1-7, 1923.
49. Bradley, S. E., Curry, J., and Bradley, G. P. Unpublished data.
50. Smith, H. W., Chasis, H., Goldring, W., and Ranges, H. A. Glomerular dynamics in normal human kidney. *J. Clin. Investigation* **19**: 751-764, 1940.
51. Lamport, H. Formulae for afferent and efferent arteriolar resistance in human kidney: application to effects of spinal anesthesia. *J. Clin. Investigation* **20**:535-544, 1941.
52. *Idem.* Relative changes in afferent and efferent arteriolar resistance in normal human kidney. *J. Clin. Investigation* **20**:545-548,1941.
53. Shannon, J. A. Kidney. *Ann. Rev. Physiol.* **4**:297-328, 1942.
54. Lamport, H. Improvements in calculation of renal resistance to blood flow. Charts for osmotic pressure and viscosity of blood. *J. Clin. Investigation* **22**:461-470, 1943.
55. *Idem.* Effects of renal resistance to blood flow on renin, angiotonin, pitressin and atropine, hypertension, and toxemia of pregnancy. *J. Clin. Investigation* **21**:685-695, 1942.
56. Oliver, J., Bloom, F., and MacDowell, M. Structural and functional transformations in the tubular epithelium of dog's kidney in chronic Bright's disease and their relation to mechanisms of renal compensation and failure. *J. Exper. Med.* **73**:141-160, 1941.
57. Bobey, M. E., Longley, L. P., Dickes, R., Price, J. W., and Hayman, J. M., Jr. Effect of uranium poisoning on plasma diodrast clearance and renal plasma flow in dog. *Am. J. Physiol.* **139**:155-160, 1943.
58. Smith, H. W. Note on interpretation of clearance methods in diseased kidney. *J. Clin. Investigation* **20**:631-635, 1941.
59. Earle, D. P., Jr., Taggart, J. V., and Shannon, J. A. Glomerulonephritis: survey of functional organization of kidney in various stages of diffuse glomerulonephritis. *J. Clin. Investigation* **23**: 119-137, 1944.
60. Wellen, I., Welsh, C. A., Taylor, H. C., Jr., and Rosenthal, A. Filtration rate, effective renal blood flow, tubular excretory mass and phenol red clearance in specific toxemia of pregnancy. *J. Clin. Investigation* **21**:63-70, 1942.
61. Lauson, H. D., Bradley, S. E., and Cournand, A. Renal circulation in shock. *J. Clin. Investigation* **23**:381-402, 1944.
62. Goldring, W., Chasis, H., Ranges, H. A., and Smith, H. W. Relations of effective renal blood flow and glomerular filtration to tubular excretory mass in normal man. *J. Clin. Investigation* **19**: 739-750, 1940.
63. Smith, H. W., et al. William Henry Welch Lecture. II. Application of saturation methods to study of glomerular and tubular function in human kidney. *J. Mt. Sinai Hosp.* **10**:59-108, 1943.
64. Shannon, J. A., Farber, S., and Troast, L. Measurement of glucose Tm in normal dog. *Am. J. Physiol.* **133**:752-761, 1941.
65. Shannon, J. A. Renal tubular excretion. *Physiol. Rev.* **19**:63-93, 1939.
66. Pitts, R. F. Renal reabsorptive mechanism in dog common to glycine and creatine. *Am. J Physiol.* **140**:156-167, 1943
67. *Idem.* Comparison of renal reabsorptive processes for several amino acids. *Am. J. Physiol.* **140**:535-547, 1944.
68. Shannon, J. A. Tubular reabsorption of xylose in normal dog. *Am. J. Physiol.* **122**:775-781, 1938.
69. Smith, H. W., Goldring, W., and Chasis, H. Measurement of tubular excretory mass, effective blood flow and filtration rate in normal human kidney. *J. Clin. Investigation* **17**:263-278, 1938.
70. Smith, W. W., and Ranges, H. A. Renal clearances of iopax, neoiopax and skiodan in man. *Am. J. Physiol.* **123**:720-724, 1938.
71. Finkelstein, N., Aliminosa, L. M., and Smith, H. W. Renal clearances of hippuric acid and pyridone derivatives. *Am. J. Physiol.* **133**: 276, 1941.
72. Rammelkamp, C. H., and Bradley, S. E. Excretion of penicillin in man. *Proc. Soc. Exper. Biol. & Med.* **53**:30-32, 1943.
73. Beyer, K. H., Woodward, R., Peters, L., Verwey, W. F., and Mattis, P. A. Prolongation of penicillin retention in body by means of para-aminohippuric acid. *Science* **100**:107, 1944.
74. Cori, G. T., and Cori, C. F. Kinetics of enzymatic synthesis of glycogen from glucose-1-phosphate. *J. Biol. Chem.* **135**:733-756, 1940.
75. White, H. L., Heinbecker, P., and Rolf, D. Hypophysis and renal function. *Am. J. Physiol.* **133**:489, 1941.
76. *Idem.* Effects of removal of anterior lobe of hypophysis on some renal functions. *Am. J. Physiol.* **136**:584-591, 1942.
77. Heinbecker, P., Rolf, D., and White, H. L. Effects of extracts of hypophysis, thyroid and adrenal cortex on some renal functions. *Am. J. Physiol.* **139**:543-549, 1943.
78. Selkurt, E. E., Talbot, L. J., and Houck, C. R. Effect of administration of estrogen on mechanism of ascorbic acid excretion in dog. *Am. J. Physiol.* **140**:260-268, 1943.
79. Ludden, J. B., Heinbecker, E., and Wright, I. S. Effect of testosterone propionate, estradiol benzoate and desoxycorticosterone acetate on kidneys of adult rats. *Endocrinology* **28**:619-623, 1941.
80. Selye, H. Effect of testosterone on kidney. *J. Urol.* **42**:637-641, 1939.
81. Korenchevsky, V., and Ross, M. A. Kidneys and sex hormones. *Brit. M. J.* 1:645-648, 1940.
82. Lattimer, J. K. Action of testosterone propionate upon kidneys of rats, dogs, and men. *J. Urol.* **48**:778-794, 1942.
83. Welsh, C. A., Rosenthal, A., Duncan, M. T., and Taylor, H. C., Jr. Effects of testosterone propionate on renal function in dog, as measured by creatinine and diodrast clearance and diodrast Tm. *Am. J. Physiol.* **137**:338-347, 1942.
84. Editorial. Relation of androgens to kidney function. *J. Clin. Endocrinol.* **3**:111, 1943.
85. Bassett, S. H., Keutmann, E. H., and Kochakian, C. D. Effect of injections of testosterone propionate on male subject with nephrotic syndrome. *J. Clin. Endocrinol.* **3**:400-404, 1943.
86. Barnett, H. L., Perley, A. M., and Heinbecker, P. Influence of eosinophile cells of hypophysis on kidney function. *Proc. Soc. Exper. Biol. & Med.* **52**:114-116, 1943.
87. Winkler, A. W., Smith, P. K., and Hoff, H. E. Absence of beneficial effects from injections of desoxycorticosterone acetate and of cortical adrenal extract in experimental anuria. *J. Clin. Investigation* **21**:419-421, 1942.
88. Selye, H., Hall, C. E., and Rowley, E. M. Malignant hypertension produced by treatment with desoxycorticosterone acetate and sodium chloride. *Canad. M. A. J.* **49**:88-92, 1943.
89. Selye, H., and Hall, C. E. Pathologic changes induced in various species by overdosage with desoxycorticosterone. *Arch. Path.* **36**: 19-31, 1943.
90. Selye, H., and Pentz, E. I. Pathogenetical correlations between periarteritis nodosa, renal hypertension and rheumatic lesions. *Canad. M. A. J.* **49**:264-272, 1943.
91. Selye, H., and Hall, C. E. Production of nephrosclerosis and cardiac hypertrophy in rat by desoxycorticosterone acetate overdosage. *Am. Heart J.* **27**:338-344, 1944.
92. Selye, H. Production of nephrosclerosis by overdosage with desoxycorticosterone acetate. *Canad. M. A. J.* **47**:515-519, 1942.
93. Selye, H., and Stone, H. Role of sodium chloride in production of nephrosclerosis by steroids. *Proc. Soc. Exper. Biol. & Med.* **52**: 190-193, 1943.
94. Selye, H., and Rowley, E. M. Prevention of experimental nephrosclerosis with methyl-testosterone. *Federation Proc.* **3**:41, 1944.
95. Hayman, J. M., Jr., and Starr, I., Jr. Experiments on glomerular distribution of blood in mammalian kidney. *J. Exper. Med.* **42**: 641-659, 1925.
96. Forster, R. P. Effect of epinephrine upon frog renal hemodynamics in intact animal. *Am. J. Physiol.* **140**:221-225, 1943.
97. Corcoran, A. C., and Page, I. H. Effects of hypotension due to hemorrhage and of blood transfusion on renal function in dogs. *J. Exper. Med.* **78**:205-224, 1943.
98. Bradley, S. E., and Bradley, G. P. Unpublished data.
99. Goldring, W., Chasis, H., Ranges, H. A., and Smith, H. W. Effective renal blood flow in subjects with essential hypertension. *J. Clin. Investigation* **20**:637-653, 1941.
100. Farr, L. E. Effect of dietary protein on urea clearance of children with nephrosis. *J. Clin. Investigation* **15**:703-710, 1936.
101. Emerson, K., Jr., Futcher, P. H., and Farr, L. E. Relation of high and low urea clearances to inulin and creatinine clearances in children with nephrotic syndrome. *J. Clin. Investigation* **20**:361-368, 1941.
102. Emerson, K., Jr., and Dole, V. P. Diodrast and inulin clearances in nephrotic children with supernormal urea clearances. *J. Clin. Investigation* **22**:447-450, 1943.

# NEW HAMPSHIRE MEDICAL SOCIETY

## PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-THIRD ANNIVERSARY

### House of Delegates, May 15 and 16, 1944 (Continued)

The next report was that of the Committee on Child Health, by Dr. Fairfield, as follows:

We recommend that the infant-care portion of the Emergency Maternal and Child Care Program be accepted under the following conditions:

That major surgical aid not be included, again because of the difficulty in determining who are "qualified consultants."

That medical aid be accepted only for illnesses requiring over two home or office visits. (This plan would eliminate many needless calls on essentially well babies and would eliminate a great deal of extra work involved in applying for aid, authorizing the service and approving the records for payment.)

Dr. Mullins asked whether he was correct in saying that the maternity program was not tied up directly with the maternity program previously voted on. Dr. Atchison replied that the program did not have to be accepted as a whole. The program was termed Emergency Maternity and Infant Care. The infant-care part of it was designed to take care of the sick in the first year of life and was not necessarily connected with the maternity part. But in conference with the Children's Bureau she was led to understand that most states included the infant care, and they had not refused to do so.

Dr. Mullins moved that recommendations of the Maternity and Infancy Committee be accepted. This motion was duly seconded and was carried.

*Report of the Committee on the Control of Cancer*

Last year this committee stated that the Executive Committee of the Women's Field Army would consider the advisability of using some of the money raised by the Women's Field Army for the encouragement of postgraduate study in cancer control, by offering any of the physicians associated with the New Hampshire cancer clinics an opportunity to take a refresher course. At a subsequent meeting of the committee it was voted to offer $250 for a month's study in one of the centers where cancer is a major activity. Owing to war conditions the committee thought it advisable to offer the same type of assistance for a shorter period at a proportionate remuneration for two weeks or even one week. The chairman of the committee made arrangements with the Memorial Hospital and the Presbyterian Hospital in New York City and with three hospitals in Boston, whereby contacts could be made with the visiting staffs for clinical observation, surgery and x-ray and radium therapy.

Since January 1, four physicians connected with the New Hampshire clinics have taken advantage of this offer, and all have reported most satisfactory co-operation from these hospitals. More of the forty-five or more physicians associated with the clinics are urged to take advantage of this financial assistance to improve their knowledge of cancer diagnosis and treatment.

The usual three short letters from your committee have been sent to all the physicians in the State. The first one called attention to the importance of blood studies in the diagnosis and treatment of cancer, particularly in patients with tumors of lymph nodes in order to detect the possible presence of leukemia, and also stressed the importance of differentiating anemias from some types of cancer, particularly cancer of the stomach. Attention was also called to the importance of blood studies with special reference to the indication for the need of transfusions in surgery of cancer patients, and in prolonged x-ray therapy. The second letter discussed the diagnostic significance of vaginal bleeding and of the differential diagnosis between carcinoma of the fundus and carcinoma of the cervix, with suggestions for procedures in making the clinical diagnosis. The third letter briefly discussed cancer of the lung with its symptoms, diagnosis and treatment, and emphasized the frequency of cough as an early symptom, the importance of an x-ray film in suggesting disease and the necessity of following this up with bronchoscopy. Copies of all our past letters have been requested by the Virginia Cancer Foundation for use in that state in their program of cancer education among the physicians.

The fourteen diagnostic clinics and treatment centers examined and treated about the same number of patients as in the previous year. Probably most of the patients who need to come for treatment have eventually arrived at one or another clinic, but it has been found that some of them have delayed coming on account of transportation difficulties, and also patients have not been able to return for checkups as frequently as they should for the same reason. It should be borne in mind that the Women's Field Army will, on application, provide some method of transportation for these people.

The Women's Field Army is also distributing the usual number of educational pamphlets, especially during the month of April, which has been designated Cancer Control Month by the Congress of the United States. They also have furnished many indigent patients with cancer dressings that are made up from linen and cotton collected from the public.

The American Society for the Control of Cancer is sponsoring cancer education in secondary schools in a large number of states throughout the country. In co-operation with educational authorities, some type of cancer instruction has been introduced into many high schools and junior high schools. It has been found that not only are young people interested, but their knowledge of cancer as it is taught in the schools, based primarily on courses in biology, is of definite benefit in instructing the older people in their families. It has been found that both students and teachers are interested in this activity, and here in New Hampshire we have found much interest and a definitely favorable response from the showing of cancer films in the high schools.

Your committee would like an expression of approval of cancer education in the secondary schools of this state before it is taken up as a state-wide project with a larger group of school administrators. We also request continued co-operation on the part of all physicians in the State in responding to requests for physical examinations. This is one phase of the work of the Women's Field Army that is stressed constantly in their literature and in the contacts of the workers with other women.

Your committee has spent $43.40 on printing, stationery and postage. The balance of our $50 appropriation has been returned to the treasurer. We respectfully request an appropriation of $50 for the coming year.

GEORGE C. WILKINS, *Chairman*
RALPH E. MILLER
GEORGE F. DWINELL, *Secretary*

Dr. Mullins suggested that the appropriation of $50 be continued and moved the adoption of this portion of the report of the Committee on Officers' Reports. This motion was duly seconded and carried.

*Report of the Committee on Medical Education and Hospitals*

The activities of this committee have been necessarily limited. This is due in the first place to the fact that there have been no fellowships offered by the Commonwealth Fund under present war conditions, presumably because there would be so few men with either the age eligibility requirements or the available time.

The committee has collaborated with various regional and national agencies and committees in surveys pertaining to postwar training opportunities that might be available or might be established in the State or the New England area.

The Speakers' Bureau has been used by a few county societies, and this activity is being continued so far as there is a demand.

The only positive activity of the chairman has been the appointment to membership on the Regional Committee of the Wartime Graduate Medical Program. Region No. 1 consists of Maine, New Hampshire, Vermont and Massachusetts. This committee has been actively engaged in the arrangements of programs at the various military stations in the region. These programs have been organized as a result of a survey of the various commanding officers to line up the topics that seem most desirable to them. These meetings have been held at frequent intervals, and once each month a bulletin announcing all meetings is issued. The speakers for these programs have been obtained by this committee. These meetings have been primarily for the men in military service within the district of the meeting, but they have also been open to civilian physicians. It is probable that this program will be continued indefinitely.

JOHN P. BOWLER, *Chairman*
JAMES W. JAMESON
HERBERT L. TAYLOR

Dr. Mullins moved the adoption of this report. This motion was duly seconded and was carried.

*Report of the Committee on Medical Preparedness*

The only activity of this committee has been to assist in the relocation of physicians to care for the civilian needs. In two cities attempts have been made to work out plans so that one doctor will be on duty each night. The doctors will take turns in this work, so that the others may secure more sleep.

DEERING G. SMITH, *Chairman*
Ezra A. Jones
CARLETON R. METCALF

Dr. Mullins moved the adoption of this report. This motion was duly seconded and was carried.

*Report of the Committee on Mental and Social Hygiene*

New Hampshire has more agencies and, when filled, a larger number on the staff of these agencies in the performance of social and mental hygiene than ever before. The blind and partially blind, the hard of hearing and the deaf all receive attention. The crippled children, the shut-in and the handicapped adults receive attention from a variety of agencies, and some of the activity on their behalf is from voluntary contributions. Through the efforts of our governor, state employees and inmates of state institutions are having x-ray films of the chest for the detection and treatment of tuberculosis.

There are other fields of human misery less well covered. Our state has many intelligent sufferers from chronic arthritis who are poor and unaided. Many of our general hospitals could be relieved of patients much more expeditiously if there were available in the State a number of good and not too expensive convalescent homes. Institutions are not desirable if they can be avoided, but we must depend on other states for the instruction of our blind and deaf, and we have no institution for the care and treatment of patients suffering from epilepsy, of whom there are a large number in our other institutions.

The absorption of the young men and women of the State by war emphasizes to the trained observer the frequency in the remaining population not only of senile persons but of psychopathic personalities. We know that the number of senile persons in proportion to the population has increased, and it is probable that pathologic personalities are also on the increase. These persons are neither fully insane, feebleminded or epileptic, but nevertheless they are not normal and it is unfortunate that they receive no recognition but with those with senile dementias are committed to the State Hospital and burden the space intended for the acutely insane.

We have many special agents, but there are very few psychiatric social workers in the State. We are seriously wanting in psychologists, and in our rural districts there are many psychotic persons who with their families would be greatly benefited by a little special psychiatric advice.

To use the numerous mental tests for the diagnosis of mental deficiency and derangements there should be several psychologists available to the school departments, and in the near future some competent analyzers of human aptitudes are needed to aid in the educational field and rehabilitation. An amount of this work, relatively small in comparison with the needs, has been furnished by the colleges, by the Laconia State School and principally by the State Hospital. The performance of this work calls for support from some source, and it may be properly questioned whether or not state institutions and colleges should be the source of this support, or whether clinics should be publicly maintained.

The sensible publicity approach to venereal disease has been highly advantageous, and we believe that its treatment is much more general and effective than it was some years ago. So far as we can learn, the law requiring blood examination before marriage is properly complied with and fairly efficiently. The law permitting sterilization of the insane, feeble minded and epileptic in institutions is operating conservatively, and we hope in conformity with the letter of the law, which permits operation in hereditary and transmissible cases.

Unknown to many, the State has a law that was intended to limit the marriage of defective persons and is found in Chapter 286 on page 1164 of Volume II of the Public Laws of 1926. As near as we can learn, this law is practically ignored. A few clerks have refused licenses and referred the parties to the State Board of Health for an examination. Under this law it is the duty of all superintendents of schools and all having charge of instruction in private schools and state institutions to report the names of all defectives discharged through those sources. The intention of the law is that the names of those persons be kept on file in the Bureau of Vital Statistics and be available there not only for reference by city clerks but as accumulating data on the number of such persons in the State and for the detection of hereditary families. It is not evident that this part of the law is complied with. There are now 700 inmates at Laconia State School and this is probably not more than 12 per cent of the mentally deficient in the State. We have compiled for years vital statistics, but no one knows how many mentally deficient there are in New Hampshire.

B. W. BAKER, *Chairman*
CHARLES H. DOLLOFF
JOHN B. MCKENNA

Dr. Mullins for the Committee on Officers' Reports agreed that there is a need for more specialized workers in mental and social hygiene in this state, and that proper presentations should be made through the appropriate channels to the State Legislative Assembly in 1945. He moved the adoption of this portion of the Report of the Committee on Officers' Reports. The motion was duly seconded and was carried.

*Report of the Committee on Public Health*

This, the third year of this committee, has been uneventful. In spite of the increase in activity in industrial fields throughout New England, we of New Hampshire have experienced proportionately a very small increase in man-

power along industrial lines, and this is particularly true if one eliminates the Portsmouth area, where so many citizens have been employed in the Portsmouth Navy Yard, together with the lumber centers in the northern section of our state. For this reason, the industrial public-health situation in New Hampshire has presented a very minor problem as compared with that in some of the more active centers of manufacture in other sections of the country.

The housing situation in and around Portsmouth has caused some anxiety, but this has been greatly relieved by the daily transportation of employees to and from their work.

As a result of the previous programs of the Committee on Public Health, we feel that the groundwork of this committee is well established. We believe that the health of industrial employees in this state ranks high and that the standards under which the employees work and live are among the best. This is substantiated to a large degree by the minimum number of absentee records among the employees, and this takes into consideration the fact that some of the employees travel many miles a day to and from their place of employment and also that the average age of employees has increased owing to the drafting of the younger men.

Your committee has had no reference from either employers, employees or other sources during the entire year, and this again speaks well for our working conditions and health standards, and accounts for the inaction of this committee.

We have received regular communications in connection with industrial hygiene as published by the United States Public Health Service, together with outlines of programs from various industrial centers.

Unfortunately, your chairman was unable to attend the Sixth Annual Congress on Industrial Health, which was held in Chicago in February of this year, owing to the uncertainty of family affairs at that time, and as yet we have not received the proceedings of this meeting, so consequently are unable to give you the particulars at this writing.

In submitting this report, may we state that it has been a pleasure to serve on the Committee on Public Health of the New Hampshire Medical Society and, although the duties have been somewhat limited, we feel certain that there will be more and more problems presented to this committee as time goes on.

HARRIS E. POWERS, *Chairman*
ANTHONY E. PETERS
CLINTON R. MELLIN

Dr. Mullins said that the Committee on Officers' Reports was pleased to note the high standard of public health in New Hampshire. The fact that no complaints have been voiced was a good indication that conditions were satisfactory. He moved the adoption of this report. This motion was duly seconded and was carried.

### *Report of the Committee on Tuberculosis*

It is with deep regret that the Committee on Tuberculosis records in this report the death on March 30, 1944, of one of its members, Dr. Clarence O. Coburn, of Manchester. For thirty-eight years Dr. Coburn had been engaged in the private practice of medicine in his native city. He had devoted his practice to internal medicine, in which field he was widely recognized for his unusual skill, judgment and resourcefulness. A tried and true physician, Dr. Coburn was at all times one who exemplified the finest ideals in citizenship and service to his fellow men. During the years 1919 to 1921 he was president of the New Hampshire Tuberculosis Association. His active interest and support in the campaign against the disease was maintained until the end. His death is a sad and severe loss to this Society and particularly to the Committee on Tuberculosis.

As has been stated in previous reports, the encouraging progress that has been made in combating tuberculosis in New Hampshire is due largely to the efforts of the members of the New Hampshire Medical Society. The physicians of New Hampshire are the first line of defense and attack in the fight against the disease. They are the "case finders" par excellence in the program of early diagnosis, particularly of open cases, in which prompt supervision and treatment are of utmost importance.

During the past year a larger number of possible tuberculous patients than for some years past have been referred to the chest diagnostic clinics maintained throughout the State. It is felt that these clinics perform their greatest service when they assist the members of the New Hampshire Medical Society in the diagnosis of tuberculosis among their patients who present suspicious signs and symptoms.

An excellent piece of tuberculosis case finding continues to be carried on at the Selective Service induction center in Manchester. An essential part of the exacting examinations at this induction center is an x-ray examination of the chest for every man. All men found to have roentgenographic evidence of tuberculosis are afforded prompt follow-up. In this way, the Selective Service Boards are not only keeping tuberculosis out of the military forces but are also providing a splendid case-finding program for a sizable segment of the population of our state.

Since June, 1943, the chests of approximately 4500 workers in the industries of this state have been examined roentgenographically. This has been accomplished through a joint program inaugurated and maintained by the Industrial Hygiene Division of the State Department of Health and the New Hampshire Tuberculosis Association. The remarkable success of this program is due to the whole-hearted cooperation of management and labor, including industrial physicians and labor organizations. This program is resulting in the discovery of large numbers of potentially active cases of tuberculosis. The program is progressing rapidly.

For some years your committee has emphasized the great value of the chest roentgenogram in the discovery of tuberculous patients. It is well known that tuberculous lesions can be seen in the chest roentgenographically before signs can be heard with the stethoscope. We again urge the members of the New Hampshire Medical Society to use the roentgenographic method frequently when examining chests. The New Hampshire Tuberculosis Association is ready to provide chest x-ray films for persons referred by physicians when these persons are unable to pay for them. Furthermore, the New Hampshire State Sanatorium and the New Hampshire Tuberculosis Association continue to offer their services in the interpretation of chest x-ray films sent to them for diagnosis.

We also urge prompt examination of all members of the family when a case of tuberculosis is found, since in a household where an open case has been discovered we usually find that all members are positive tuberculin reactors.

We also urge at least a tuberculin test for all persons caring for children. This should be a routine procedure for nursemaids, governesses and others in contact with children.

In the treatment of tuberculosis, bed rest continues to be emphasized. It is generally considered that a bed-rest regime is extremely helpful in deciding on the clinical activity of the disease. Surgical procedures such as pneumothorax phrenicotomy, phrenicotomy and thoracoplasty are still employed in properly selected cases as aids to the cure of the disease.

Beginning July 1, 1943, the appropriation for hospitalization of tuberculosis cases under the advanced case appropriation was transferred from the State Department of Public Welfare to the State Department of Health. Applications for admission of patients to the Pembroke Sanatorium are now sent to the State Department of Health. The medical supervision of the patients at the Pembroke Sanatorium is therefore under the jurisdiction of the State Department of Health.

Dr. Rufus R. Little, superintendent and medical director of the New Hampshire State Sanatorium at Glencliff, has been appointed consultant on tuberculosis to the State Department of Health. This program has proved extremely helpful, and the work of the two sanatoriums is now splendidly co-ordinated. Dr. Little visits the Pembroke Sanatorium once a week. Once in three weeks, chest surgery is performed at the Glencliff Sanatorium for patients from both institutions. These operations comprise thoracoplasty, lobectomy, phrenicectomy and so forth. Pneumothorax is a routine procedure at both sanatoriums.

Our nation is now in the final stages of the second great war. It appears that up to the present time there has been no increase in the number of deaths or the death rate from tuberculosis in New Hampshire. The number of *known* cases has

increased, but not the *known active* — so-called "open" — cases of tuberculosis. Because of the careful x-ray chest surveys at the Induction Center by the War Department, and among workers in industry by the State Department of Health and the New Hampshire Tuberculosis Association, a definite increase in known tuberculosis cases has been recorded. Although these cases are mostly in the arrested stage, they nevertheless constitute a potentially active source of the disease. The necessity for proper medical advice and supervision in such cases is obvious.

The fact remains that tuberculosis and war are still allies. Infection with tubercle bacilli is still widespread among the people. Tuberculin-test surveys indicate that approximately 50 per cent of the adult population of our state harbor tubercle bacilli. The infection is held in abeyance in many cases because of adequate physical resistance on the part of those who are infected. Longer hours of labor and increased mental and physical strain tend to lower physical resistance, thereby predisposing toward the breakdown of a previously quiescent or so-called "healed" lesion. To use the layman's words, tired bodies may permit the ever-lurking tuberculosis germs to attack the lung cells successfully.

There must be no relaxation in the fight against the tubercle bacillus. In fact, the fight must be carried on with ever greater aggressiveness to hold the gains won.

Your committee avails itself of this opportunity to express its deep sense of gratitude and appreciation for the wholehearted assistance and encouragement accorded to it by the members of the New Hampshire Medical Society.

ROBERT B. KERR, *Chairman*
RICHARD C. BATT

Dr. Mullins for the Committee on Officers' Reports congratulated the Committee on Tuberculosis on its excellent and inclusive report. The change of administration from the Department of Public Welfare to that of Public Health seemed to him a proper step. The suggestion of more frequent use of the x-ray in suspected cases of tuberculosis was particularly commended. Dr. Mullins moved the adoption of this report, and the motion was duly seconded and was carried.

### *Report of the Delegate to the House of Delegates of the American Medical Association*

The annual session of the American Medical Association was held at Chicago, June 7, 8 and 9, 1943, and was limited to meetings of the House of Delegates and to two general meetings. Your delegate served as chairman of the Reference Committee on Reports of Officers. He has endeavored to select the high points of the meeting for this report to the New Hampshire Medical Society.

Elliott P. Joslin, of Boston, was given the Distinguished Service Award and Herman L. Kretschmer, of Chicago, was chosen president-elect.

The Committee on Planning of Postwar Medical Services was established, to co-operate and collaborate with other agencies concerned with these problems.

The Board of Trustees made a lengthy report dealing with hospital corporations engaging in the practice of medicine. That the Blue Cross plans to give medical service with or without the approval of the medical profession there can be no doubt after reading this report. It was voted that hospitals should not be permitted to practice medicine, and the House reiterated its disapproval of the injecting of a third party into the personal relation of the patient and the physician. It further voted "that the practice of radiology, pathology and anesthesiology is the practice of medicine just as much as is the practice of surgery or internal medicine, and that it is only a short step from including the first three in a medical-service plan to including the whole field of medicine in such a plan."

The Council on Medical Service and Public Relations was established. The functions of this council are as follows: to make available facts, data and medical opinions with respect to timely and adequate rendition of medical care to the American people; to inform constituent associations and component societies of proposed changes affecting medical care in the nation; to inform constituent associations and component societies regarding the activities of the council; to investigate matters pertaining to the economic, social and similar aspects of medical care for all the people; to study and suggest means for the distribution of medical service to the public consistent with the principles adopted by the House of Delegates; to develop and assist committees on medical service and public relations originating within the constituent associations and component societies of the American Medical Association.

The action of the federal government in making funds available for maternity and infant care for the wives and infants of enlisted men was approved, and adoption was urged of a plan under which the federal government would provide for the wives of enlisted men a stated allotment for medical, hospital, maternity and infant care similar to the allotments already provided for the maintenance of dependents, leaving the actual arrangements with respect to fees to be fixed by mutual agreement with the wife and the physician of her choice. This action was similar to that taken by the New Hampshire House of Delegates last May. A copy of the resolution urging that the method of making available these funds be changed to an allotment basis was sent to each congressman and each senator. (After considerable discussion in the House of Representatives, the proposal was rejected by a vote of 115 to 8.)

The Board of Trustees in its report devoted considerable space to the subject of prepaid medical service. It gave the history of the various plans and discussed the progress that had been made under them. This report was published in the April 24, 1943, issue of the *Journal of the American Medical Association*. In view of the present discussion of a prepayment medical plan in our state, it seems advisable to point out some of the dangers and complications of such a plan. These were first included in a special report, approved by the House of Delegates in 1935, and seem no less applicable today than at that time; they are as follows:

The adoption and operation of a medical plan where it is unnecessary.

The stimulus aroused by good plans among irresponsible organizers to develop and operate imitations and counterfeits.

The establishment in medical practice of dangerous patterns, following the adoption of undesirable types of plans.

The compromise of medical societies in the corporate practice of medicine or in the operation of insurance companies as a result of an insufficient study of state statutes and case law.

Failure, in the operation of a plan, to conform to the *Principles of Medical Ethics*.

The almost inevitable transition of voluntary insurance plans into compulsory contributory sickness insurance systems operated by the state.

The difficulties involved in the failure adequately to provide for complete control of medical affairs by the medical profession.

The "freezing" of medical fees at a point below that which is consistent with good medical care.

Failure to bear constantly in mind that a medical society plan is an experiment in the methods of distributing medical service and that it may have only a temporary usefulness, may need frequent or drastic modifications or may need to be discarded entirely.

Medical society plans must not be considered or accepted as a substitute for the regular practice of medicine as applied to the majority of people. If it is believed such plans may be useful, they should be considered merely as supplementary facilities in the distribution of medical service. They should be used only so long and in such a manner as they serve efficiently to make more easily available to low-income groups a high quality of medical care.

The April 29, 1944, issue of the *Journal of the American Medical Association* contains the report of the Board of Trustees for the past year. It is stated there: "The population group that has incomes too small to meet health necessities in the way of food, clothing, fuel and shelter cannot be expected to budget or make prepayments for catastrophic

illness. These 'medically indigent' are always more of an economic than of a medical problem, since their medical care, regardless of the manner by which the cost is met, must, as always, be paid for directly or indirectly out of higher incomes." The necessary legislation has been secured and administrative organizations for the operation of prepayment plans are functioning in 14 states, and some part of the program has been undertaken in ten additional states. These plans have been in operation from a few months to seven years, but the demand for the service is apparently slight, for with the exception of Michigan a very small proportion of the population is enrolled. The figures given are as of 1943, in most instances the latter part of the year: California, 88,000; Colorado, 5,000; Massachusetts, 23,000; Michigan, 600,455; Missouri and Kansas, 6,500; New Jersey, 15,000; New York, 17,000 (with 22,000 in a second plan, and 5,000 in a third plan); North Carolina, 13,031; Pennsylvania, 8,500; and Texas, 378. It is evident that prepayment medical plans are still in the experimental stage, and it seems as if the New Hampshire Medical Society should consider further the advisability of launching its plan at this time.

DEERING G. SMITH

Dr. Mullins for the Committee on Officers' Reports expressed indebtedness to Dr. Smith for a thought-provoking summary of the actions of the American Medical Association. He added that consideration of these facts should guide the Society in its decisions regarding the various programs being instituted by the federal government. He moved the adoption of this report. This motion was duly seconded and was carried.

(*To be concluded*)

---

## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

### CASE 30391

#### PRESENTATION OF CASE

A fifty-nine-year-old engineering executive was seen at home because of difficulty in breathing.

The patient had always been active. While in college he had a tendency to have rapid or irregular heart action, which occasioned interest but did not bother him. At the age of forty, however, after a trip, he was seized by his first attack of palpitation. The heart action was forceful and rapid, and the attack lasted for half an hour after dinner. Since then he had had a great deal of palpitation, mostly thumps or skips but occasionally spells of heart racing (usually regular). The palpitation was especially apparent when he was tired and at rest. Examination of the heart during these attacks showed extrasystoles. The blood pressure was 135 systolic, 80 diastolic. An electrocardiogram at the age of forty-eight showed a normal rhythm with a rate of 92. The PR interval was 0.20 second, the QRS interval 0.06 second, and the T waves upright in all leads; the axis was normal. The following year he had an attack of ureteral colic on the right. The heart sounds at that time were poor. There was a definite third sound, as well as gallop rhythm, which was marked in the upright position. The blood pressure was 150 systolic, 100 diastolic. An electrocardiogram a year later showed a normal rhythm with a rate of 100, a PR interval of 0.24 second, slight left-axis deviation and frequent premature ventricular beats. These findings persisted for the next two years. There was no pain at any time. Two years later a slight presystolic gallop rhythm was heard at the apex. Frequent premature beats were present. The blood pressure was 160 systolic, 100 diastolic. At another examination he had a bigeminal pulse. The heart rhythm was definitely coupled with an extrasystole every other beat. The blood pressure was 150 systolic, 85 diastolic. An electrocardiogram showed normal sinus rhythm, a rate of 94, a PR interval of 0.24 second and a QRS interval of 0.08 second. $T_1$ and $T_2$ were low, and $T_3$ upright. There was slight shift of the axis to the right. Ventricular extrasystoles were present throughout the record, giving it a bigeminal rhythm. He was given potassium iodide for two or three months, with rest, and felt much better. The heart was regular and rapid. When fifty-five years old he had lobar pneumonia. He was hospitalized for three weeks, and during this illness "his heart did beautifully." A gallop rhythm or third sound persisted. The blood pressure was 120 systolic, 80 diastolic. Six months later he experienced irregularity of the heart beat associated with a desire to take a deep breath. He was given 0.2 gm. of quinidine twice a day for ten days, with definite benefit, but he was then hospitalized.

Examination on admission showed slight cyanosis. The left border of cardiac dullness was 14 cm. to the left of the midline. The heart was rapid but regular. The sounds were of poor quality. There was pulsus alternans, with a marked protodiastolic gallop at the apex. The pulmonic second sound was greater than the aortic. There were wheezes throughout both lung fields, with medium moist rales at the right base. The blood pressure was 145 systolic, 95 diastolic. The blood counts were normal. The

*On leave of absence.

basal metabolic rate was normal. An electrocardiogram revealed ventricular premature beats interrupting sinoauricular tachycardia at a rate of 115. There was slight auriculoventricular block, with a PR interval of 0.22 second. The QRS waves were of low voltage, slurred and slightly widened. The T waves were low in all four leads.

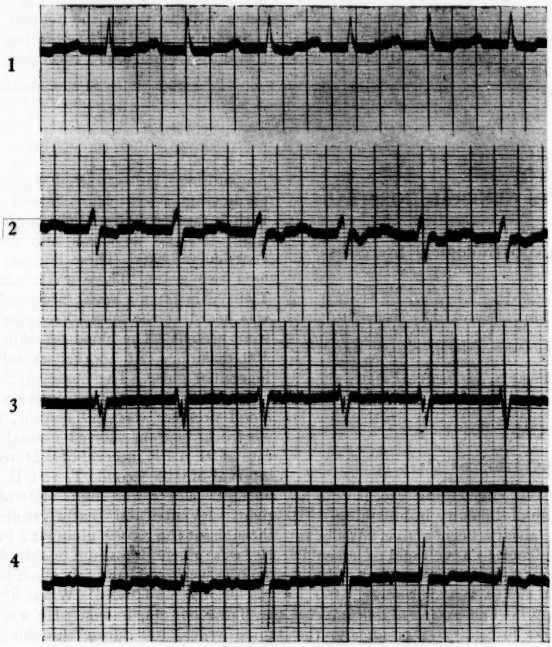


FIGURE 1.

The patient was given aminophyllin and sedatives as desired. After two weeks of bed rest he showed a rising pulse rate (130), persistent rales in both lungs and, except when taking aminophyllin, Cheyne–Stokes respirations. He was given 0.4 gm. of digitalis for four days and then 0.03 gm. daily. At the end of that period he woke up early one morning with a dull ache in the right groin which extended down to the knee and lasted for several hours. The leg seemed to buckle under him. Examination of the leg was negative. An electrocardiogram (Fig. 1) showed a PR interval of 0.3 second, a rate of 90, slight inversion of $T_1$, $T_2$ and $T_4$, and slurred QRS complexes in Leads 1, 2 and 3; there was an increase in voltage over the previous records. His condition steadily improved until the twenty-eighth hospital day, when, on moving, he suddenly had a sharp, stabbing, fleeting, nonradiating pain in the left anterior chest without interference to breathing. On questioning, he stated that he had experienced a similar pain in the right chest the previous night. Examination was negative except for a presystolic and a protodiastolic gallop. The heart sounds were of very poor quality; the second sound was almost inaudible. The blood pressure was 135 systolic, 90 diastolic. In the next ten days his condition improved considerably, the gallop rhythm became hardly noticeable,

and he was discharged on the forty-sixth hospital day.

In the course of the next three and a half years he felt well, although he became fatigued rather easily and was conscious of the irregularities of his heart beat and breathing. On such occasions a gallop rhythm was present. At all other times, the heart was rapid but regular, the sounds were of good quality, and there were no murmurs. Distended neck veins were occasionally seen. During most of that period he received digitalis, phenobarbital and Nembutal.

Following a severe upper respiratory infection from which he slowly recovered, he developed dyspnea and Cheyne–Stokes breathing at night. There was pulsus alternans, and the heart rate was 120. The blood pressure was 115 systolic, 80 diastolic. He was further digitalized. Nocturnal dyspnea and Cheyne–Stokes breathing disappeared in about two weeks. The pulsus alternans could not be heard, but there were four definite sounds in the cycle. The pulse, however, remained high. He continued to take 0.03 gm. of digitalis daily. It was decided that he should retire from his business.

The next month, following the emotional strain of selling his home and closing his business, he again developed nocturnal Cheyne–Stokes breathing. Examination showed slight dyspnea. The pulse was regular at 108. The blood pressure was 150 systolic, 115 diastolic, with evidence of pulsus alternans. Both arterial and venous pulsations were slightly increased in the neck. The cardiac impulse was felt 12 cm. to the left of the midsternal line in the sixth intercostal space. Marked diastolic gallop rhythm was present. A slight apical systolic murmur was heard. The pulmonic second sound was increased. The lungs were clear except for persistent fine rales at both bases. The liver was palpable two finger-breadths below the costal margin but was not tender. There was no edema. The patient was given 1 cc. of Salyrgan, and the fluid intake was limited to 1200 cc. There was good diuresis. Cheyne–Stokes breathing continued, however, and one week later basal rales were again heard. He was given 1 cc. of Salyrgan and theophyllin intravenously every fourth day, and 0.2 gm. of aminophyllin after each meal. He improved considerably during the next ten days. The following morning he awoke and was unable to speak clearly, to feed himself or to recognize simple objects, such as a fork and a spoon, or what to do with them. He was, however, conscious of his disability, a little agitated and somewhat confused. Neurologic examination a few hours later, during which time he had improved considerably, showed much difficulty in co-ordination and in use of the right arm and, to a less extent, of the right leg, without any particular weakness. The reflexes of the right arm and leg were slightly more active. The abdominal reflexes were absent on the right. The plantar reflexes were normal. No sensory disturbances could be made out, but there was definite stereognosis, more on the right than on the left. The cardiac situation was about the same, with the rate about 100.

During the course of the next five days the neurologic symptoms improved, and in the following two days he had nausea and retching without pain or fever. Digitalis was stopped. Examination of the heart showed galloping, with a slight apical systolic murmur. The sounds were weak, and the rate was 110, with slight pulsus alternans and occasional premature beats. The blood pressure was 140 systolic, 100 diastolic. The lungs were clear. He was placed in an oxygen tent. He became restless and developed marked cyanosis, the Cheyne–Stokes breathing increased, with periods of apnea lasting forty to sixty seconds, and he died four days later.

## Differential Diagnosis

Dr. Conger Williams: So far in discussing these cases I have had a perfect score — 100 per cent wrong. I am sure that this case will be no exception.

Up to ten years before the final episode, this man had had no definite evidence of heart disease. It is true that he had had numerous episodes of palpitation and possibly even paroxysmal tachycardia of unknown kind, but as everyone knows, that is a frequent finding with a normal heart. I am sure that up to that time he had had no significant heart disease.

"The PR interval was 0.24 second." In that statement lies the answer to the gallop rhythm. Gallop rhythm may or may not have a serious prognostic significance. If the gallop is the result of a weakened myocardium, it may be extremely important. On the other hand, it is well to remember that in the presence of a long PR interval the distance between auricular and ventricular contraction is increased and therefore it is often possible to hear the auricular sound as a separate sound, in which event gallop rhythm is produced. That is undoubtedly the case here because the rhythm lasted ten years, and it is unusual to have gallop rhythm due to myocardial weakness last that long. At that time there occurred the first evidence of disease of the cardiovascular system, in that he was developing hypertension and evidence of auriculoventricular block.

"At another examination he had a bigeminal pulse." This finding is not necessarily significant since we know that he had been subject to ectopic beats most of his life.

The electrocardiogram taken at the age of fifty-one was abnormal in that $T_1$ and $T_2$ were low. I do

not believe that the slight shift in axis to the right was significant.

I presume that the potassium iodide was given for arteriosclerosis rather than for syphilis or goiter. Whether quinidine was given to cut down on the number of ectopic beats, or whether he actually had a paroxysmal arrhythmia, such as fibrillation, I cannot say from the evidence.

The finding of pulsus alternans at the age of fifty-five was really the first definite evidence of myocardial weakness. It is an important finding as a rule, and in this case had special significance because the gallop rhythm during the first few years of observation was not the result of a weakened myocardium.

The rising pulse and the lung findings may have represented increase in cardiac failure in spite of the fact that he was kept at bed rest and given treatment. I do not know why the giving of digitalis was delayed so long unless it was thought that the lung findings were due to something else.

The cause of the attack of pain in the right leg is not apparent. He might have had thrombophlebitis giving a transitory episode of pain or possibly a small arterial embolus from the heart that set up generalized vasospasm, a not uncommon occurrence; it is possible for such a small embolus to break up subsequently and to be distributed throughout the vascular tree, leaving no evidence of arterial occlusion on subsequent physical examination.

I presume that the pain in the anterior chest was not related to breathing. The fact that he had had similar pain on the previous night, however, is evidence in favor of the diagnosis of thrombophlebitis. This might well have represented a small pulmonary embolus first to the right lung and then to the left. He had been in bed for at least two weeks before this happened, and the pulmonary episode apparently followed the development of pain in the leg. It is also possible that the dyspnea at the time of admission and the finding of rales at both lung bases represented an earlier pulmonary embolus.

It is obvious that toward the end he had some sort of destructive lesion involving the left side of the brain. It could have been an embolus but most likely was a thrombus or hemorrhage. The sudden onset and the rather rapid clearing are in favor of a vascular episode.

A few things are fairly certain. We have a patient, fifty-nine years of age, who for the last ten years of his life had had partial auriculoventricular block, and for the last three and a half years, cardiac failure. He also had several other episodes, some of which may have been embolic. That much of the story is fairly certain, but from then on to discuss the etiology is simply conjecture.

One diagnosis that might fit most of the findings is that of hypertensive and coronary heart disease. Involvement of the coronary arteries could well explain the long duration of auriculoventricular block, which is not exceptional. The electrocardiogram is entirely in keeping with a diagnosis of coronary heart disease. It is also possible that at some time in his career the patient had had myocardial infarction, although we have no specific evidence either clinically or by electrocardiogram to support this diagnosis. One thing that made me consider that possibility was the large size of the heart. It seemed just a little too large to be explained by hypertension of mild degree, even though it had lasted for ten years. Another point that made me consider the diagnosis of myocardial infarction was the fact that he had had several episodes, more particularly the last one, suggesting embolism. An embolus could have gone to the brain from the heart wall and produced the terminal neurologic changes. Of course the embolus, if he had one, might have come from the auricle. As in every cardiac death, the question of pulmonary embolus must be considered. I cannot rule it out, although I think it is unlikely. Whether or not he had a slight degree of chronic cor pulmonale on the basis of an old embolus also cannot be decided on the evidence presented. It is possible that he had an arterial embolus at the time of his first really severe illness, when he developed pain in the legs. Where that came from is another matter for conjecture.

What else could fit in with a picture like this? In these conferences a time always comes, after the likeliest diagnosis has been considered, when one should consider unusual diagnoses. Accordingly, in this case, I think that we should at least consider a cardiac tumor. It is well known that primary cardiac tumors may produce prolongation of the PR interval, either from interference with the arterial supply or by direct pressure over a long period of time. By direct invasion of the myocardium they may also produce cardiac enlargement and congestive failure. Cardiac tumors that grow on the endocardial surface may give rise to emboli when portions of the tumor break off. It is usually not possible to make a diagnosis of tumor, especially primary tumor, unless one has been fortunate enough to note the syndrome that is caused by the tumor's projecting into the cavity of the left auricle and causing paroxysmal obstruction of the mitral orifice. In such cases patients have a characteristic dyspnea, which is present while the patient is in the upright position and disappears when the horizontal position is assumed. I do not believe, however, that the diagnosis of tumor should be seriously considered here.

The rare forms of heart disease, such as beriberi and periarteritis nodosa, do not fit too well into this long, chronic course. So I shall stick to my first diagnosis: hypertensive and coronary heart disease,

with cardiac enlargement, congestive failure and partial auriculoventricular block and possibly thrombophlebitis and pulmonary embolism, as well as cerebral embolism.

DR. PAUL D. WHITE: I saw this man several years before he died, and although I had heard from him in the meantime, I did not see him again until a few weeks before he died. I had not the faintest idea why he had auriculoventricular block. At first, the late Dr. Breed, whose patient he was, and I thought that he probably had coronary heart disease. He also had, however, a little hypertension, and I did not know how much of a role that might have played. He continued to have a slight to moderate amount of hypertension throughout the last ten years of life, and during the latter part of his life, especially the last three weeks, he had intractable congestive failure. Undoubtedly the earlier gallop rhythm, as Dr. Williams said, was due to auriculoventricular block and that is what we ascribed it to, undoubtedly presystolic at that time. Later the patient had a clear-cut pulsus alternans and extra sounds but no murmurs; we then ascribed the fourth sound early in diastole to dilatation of the heart, which was justified because he had both types of gallop rhythm. My final diagnosis agreed with that of Dr. Breed — coronary and hypertensive heart disease, with intractable failure. I thought that the cerebral vascular accidents were embolic rather than hemorrhagic.

DR. CHESTER M. JONES: Is there anything in the x-ray films of the chest that suggests pulmonary embolism?

DR. LAURENCE L. ROBBINS: Not unless what was said to have been pneumonia could have been an infarct. The films are not particularly good, and there is no follow-up to tell how the pneumonia cleared.

### CLINICAL DIAGNOSES

Coronary and hypertensive heart disease.

Congestive heart failure.

Cerebral embolism.

### DR. WILLIAMS'S DIAGNOSES

Hypertensive and coronary heart disease.

Congestive heart failure.

Thrombophlebitis and pulmonary embolism?

Cerebral embolism?

### ANATOMICAL DIAGNOSES

Idiopathic cardiac hypertrophy: left ventricle.

Mural thrombi: left ventricle and right auricle.

Pulmonary infarction of right upper and left lower lobes.

Chronic passive congestion of liver and spleen.

Central necrosis of liver.

Right hydrothorax, slight.

Cerebral infarction, bilateral, old and recent.

### PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: I can tell you what we found, but I am not sure that I can name the disease this man had.

In the interstices of the trabeculae carneae of the left ventricle were thrombi that were only slightly adherent to the heart muscle itself; they could easily be picked off but had definitely occurred ante mortem (Fig. 2). The heart was enlarged, weighing 550 gm., and there was hypertrophy of the left side consistent with a moderate degree of hypertension. The coronaries, however, looked quite good. There were a few slightly atheromatous plaques but no appreciable narrowing. I am fairly certain that coronary disease itself played no part in the symptoms.

DR. WHITE: Might it be possible that the small vessels supplying the auriculoventricular junctional tissues were affected?

DR. CASTLEMAN: I doubt it because the myocardium underneath these thrombi showed no evidence of old or recent infarction. There were a few small areas of fibrosis in a few sections of the myocardium throughout the heart, but we were unable to find anything that we could call an infarct, and there was no cellular infiltration, which probably rules out Fiedler's myocarditis.[1]

DR. WHITE: The fibrosis I suppose was of other origin than coronary.

DR. CASTLEMAN: Yes. There was no intimal fibrosis such as one sees with a vitamin deficiency, although in these cases one often finds mural thrombi in the left ventricle wall such as were found here.

DR. WHITE: The prolongation of the PR interval might have been rheumatic in origin. Was there any evidence of that?

DR. CASTLEMAN: No.

A PHYSICIAN: Is it not unusual to have a PR interval of 0.3 second with rheumatic fever?

DR. WHITE: It is rare, but it does occur.

DR. CASTLEMAN: In the brain there was an old linear infarct in the right temporoparietal region.

The recent episode was a hemorrhagic infarct on the left parietal region, undoubtedly due to an embolus from the left ventricle.

DR. WHITE: Every year we have at least one case of heart disease of unexplained origin. I suppose that this is the one for this year.

DR. WILLIAMS: How about the duration?

DR. CASTLEMAN: That is against it. I believe that in the longest case of Fiedler's myocarditis the patient survived only eighteen months. Also, this man was well nourished and showed no evidence of a vitamin deficiency.

FIGURE 2.

DR. CASTLEMAN: No; several months ago we had one that was similar to this — a patient with emboli to the mesenteric vessels from cardiac mural thrombi.[2]

DR. WHITE: It hardly seems as if hypertension alone could have explained the clinical picture.

DR. CASTLEMAN: The gross appearance of the heart fits with Fiedler's myocarditis or beriberi heart.

Mural thrombi were also present in the right auricle, and there were pulmonary infarcts in the right upper and left lower lobes.

### REFERENCES

1. Fiedler, A. Über akute interstitielle Myokarditis. *Centralbl. f. inn. Med.* **21**:212, 1900.
2. Case records of the Massachusetts General Hospital (Case 30111). *New Eng. J. Med.* **230**:327-331, 1944.

## CASE 30392

### PRESENTATION OF CASE

A nineteen-year-old farmer was admitted to the hospital for study.

The patient had had pertussis, chicken pox and scarlet fever as a child but had otherwise been in good health until five months before admission, when he developed a severe sore throat and swollen lymph nodes in the neck. He felt quite ill and remained in bed. He was said to have been treated heavily with sulfonamides, of which he apparently received "three bottles" over a period of two or three weeks. The course of the sore throat was apparently not altered by the medication, and "the tonsils sloughed out." Either immediately after the drug was stopped or three to five days later, he suddenly developed itching all over the body, with

swelling of the neck and ankles and a blister on the wrist. No more sulfonamide was given. The swelling subsided in three days, and he slowly recovered in the following two or three months. He was able to work on the farm but he noted progressively increasing generalized fatigue. During the entire period he was under the observation of his family physician, who informed his mother that from time to time the patient had some albumin in the urine. There was no definite statement as to when albuminuria was first noted, and the amount was said to be "not alarming." He had received some liver and iron and had been told by his physician that he was improving and that his blood pressure was falling. Three weeks before admission, because of generalized aches, he went to bed, where he remained. One week later he developed bleeding and soreness about the base of the glans penis, and four days before entry he began to have tenesmus and bloody oozing from the rectum. There was one episode of vomiting the day before admission. He had lost a total of 20 pounds. There was no gross hematuria, increased frequency, nocturia or dysuria.

Physical examination showed a well-developed, slightly pale, chronically ill young man who was too weak to sit up. There were occasional questionable petechial lesions on the outer aspect of the left thigh. A large exudate was seen in the left fundus; the vessels were thin and there were no hemorrhages. The tongue was dry and coated. The breath was slightly uriniferous. The pharynx was moderately injected. The tonsils were small. The left border of cardiac dullness was felt 8.5 cm. from the midline. The sounds were of good quality and regular. Grade 1 apical and pulmonic systolic murmurs were heard. The lungs were clear. The abdomen was normal. There was partial hypospadias involving the glans; and a bleeding ulcer under the foreskin behind the glans. There were a few small hemorrhoids. A coarse tremor was brought out by exercise, and there was a rare spontaneous muscle twitch. The Chvostek and perineal reflexes were negative. The tendon reflexes were feeble, with a tendency to reduplication. The plantar reflexes were diminished. The sensorium was intact.

The blood pressure was 120 systolic, 75 diastolic. The temperature was 99.2°F., the pulse 86, and the respirations 20.

Examination of the blood showed a red-cell count of 2,530,000, with 8 gm. of hemoglobin. The white-cell count was 7400, with 87 per cent neutrophils. A blood Hinton test was negative. The urine was cloudy, with a pH of 5.5, a specific gravity of 1.010 and a ++++ test for albumin; the sediment contained 4 to 5 white cells, 15 to 20 red cells and rare granular and red-cell casts per high-power field and many triple phosphate crystals. The stools were guaiac positive.

A roentgenogram of the chest was negative.

The blood nonprotein nitrogen was 100 mg. per 100 cc. The carbon dioxide combining power was 19.5 millimols per liter, and the chloride 90.9 milliequiv. The uric acid was 14 mg. per 100 cc., and the blood protein 8.4 gm., with an albumin of 4.0 gm. and a globulin of 4.4 gm., an albumin-globulin ratio of 0.9. The calcium was 11.4 mg. per 100 cc., the phosphorus 22.2 mg., and the phosphatase 4 Bodansky units. The last three determinations were done on hemolyzed blood, and a repeat test for phosphorus gave a level of 16.0 mg. per 100 cc. The phenolsulfonephthalein excretion was less than 5 per cent at the end of two hours.

The patient received daily intravenous fluids, including sodium lactate. His condition steadily became worse. On the third day the nonprotein nitrogen was 128 mg. per 100 cc. For the first three days the urinary outputs were 1000, 1500 and 2000 on an intake of 1250, 2000 and 3700 cc., respectively. The character of the urine remained the same except that the pH rose to 7.5. The blood pressure was 140 systolic, 80 diastolic. On the sixth day he became semicomatose and had frequent muscle twitches. Ulcers developed in his mouth and extended into the pharynx. There were edema and swelling of the perioral tissue. The stools gave a ++++ test for guaiac, and there was a discharge of serosanguineous fluid from the oral cavity. His pulse rose to 120. The lungs, however, remained clear and the heart sounds were of good quality. The following day the urinary output fell to 500 cc. on an intake of 4500 cc. On the afternoon of that day the blood pressure fell to 110 systolic, 30 diastolic, and the pulse was 100; the patient died shortly thereafter.

## Differential Diagnosis

Dr. William Beckman: All the information in the record adds up to the fact that this man died of renal failure. From the history we learn that he had had albumin in his urine and that his blood pressure must have been elevated since his physician said it was falling. The bleeding tendency, the weight loss and the aching are also consistent with uremia.

The physical examination also provides evidence for the diagnosis of renal failure. The retinal exudate and the tremor are frequent findings, and petechial lesions are occasionally seen in uremia. Of course in the terminal stage of the disease one would have liked to note a higher blood pressure, but the normal values discovered in the hospital are certainly not incompatible with the condition.

The laboratory data confirm the impression of renal failure. Anemia is an almost constant feature, as are albuminuria and the finding of red cells and casts in the sediment. The elevated nonprotein nitrogen, the acidosis, — as evidenced by the diminished carbon dioxide combining power, — the

elevated uric acid and the marked increase in phosphorus concentration, all point toward markedly diminished renal function. I believe that with this array of evidence no other diagnosis can be supported.

Other causes of an elevated nonprotein nitrogen, such as dehydration and severe diarrhea, would not exhibit all the findings in the history and physical examination, and of course he did not have diarrhea.

Having now made out a case for renal failure, the important part of this exercise is to try to decide on the etiology of the kidney disease that was present. Of course any form of renal disease, from glomerulonephritis to amyloidosis, can lead to uremia, and it is usually difficult to tell precisely which one is present in any given case. It seems possible to rule out amyloidosis because there was no evidence of any condition, such as chronic suppuration, rheumatoid arthritis or tuberculosis, that is commonly associated with amyloidosis. Likewise one can rule out chronic pyelonephritis, since there was no evidence of an infection of the urinary tract; at least there is no report of a positive urine culture.

My first suggestion is that the streptococcal infection that he suffered five months prior to admission gave rise to an acute glomerulonephritis that remained active until death. I have no way of ruling out this possibility, but I should not expect acute nephritis to subside for a brief period and then flare up again. From the record one cannot be absolutely certain that there was a remission with a relapse, since his physician apparently found an elevated blood pressure during the period when he was well and able to work.

A second possibility is that following the scarlet fever that he had as a child he developed an acute glomerulonephritis, which had been smoldering in a latent state up to the time of the infection that precipitated the present illness. The latter infection may have exacerbated the already present nephritis and produced this picture of chronic renal failure.

A third possibility is that this patient's renal disease was the result of a reaction to the sulfonamides that he was given in fairly large quantities. A sulfonamide reaction is the only interpretation that I can think of for the attack of itching of the skin and swelling of the ankles. It has been amply demonstrated in the past few years that the sulfonamides are capable of producing renal disease, which is, I believe, of a somewhat variable nature. Rich* has reported some cases in which the patients developed periarteritis nodosa, presumably as a result of the hypersensitivity to the sulfonamide. The fact that this man had such marked muscular aching might be explained on the basis of periarteritis nodosa. Also, the petechial rash is more consistent with this diagnosis than it is with plain uremia.

*Rich, A. R., and Gregory, J. E. Experimental demonstration that periarteritis nodosa is manifestation of hypersensitivity. *Bull. Johns Hopkins Hosp.* 72:65-88, 1943

Finally, it is possible that a latent nephritis, which occurred at the time of the scarlet fever, could be exacerbated not only by the streptococcal infection but also by the sulfonamide reaction.

I have no way of differentiating the last four possibilities that I have mentioned. However, making use of the meager clinical data that I have, I shall commit myself to a diagnosis of sulfonamide reaction with resultant periarteritis nodosa.

### Clinical Diagnosis

Chronic glomerulonephritis.

### Dr. Beckman's Diagnosis

Sulfonamide nephropathy, with resultant periarteritis nodosa and renal failure.

### Anatomical Diagnoses

Chronic glomerulonephritis, with superimposed acute pyelonephritis.
Sulfonamide nephropathy?
Balanoposthitis, acute and chronic.
Cystitis.
Parathyroid hyperplasia, secondary.
Bronchopneumonia.
Petechial hemorrhages of lungs, stomach and esophagus.

### Pathological Discussion

Dr. Benjamin Castleman: The autopsy on this boy showed a small pair of kidneys, weighing 100 gm., thus indicating that the renal disease dated back for a long period of time — certainly longer than five months. Microscopic examination showed marked dilatation of the tubules, which is the best anatomic evidence that we have of renal impairment of any type. The changes in the glomerular tufts were characteristic of chronic glomerulonephritis, with numerous capsular adhesions. In addition there was a fair amount of lymphocytic and polymorphonuclear infiltration and fibrosis of the stroma.

How much the sulfonamides had to do with this uremic death is difficult to answer. There is no doubt that he received sulfonamides after his kidneys had contracted, and the drug must have been an added burden to the kidneys, which might have precipitated the acute renal failure. We have no definite evidence in the kidneys, however, that this was the case, and the findings are consistent with a chronic glomerulonephritis and a superimposed acute infection. The patient did have a mild cystitis, and further evidence that he had had renal disease for a long time was a moderate degree of secondary hyperplasia of all four parathyroid glands.

The heart was slightly enlarged and weighed 330 gm.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. Conrad Wesselhoeft, M.D.
Oliver Cope, M.D.

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

Editorial Board

Joseph Garland, M.D. A. Warren Stearns, M.D.
Shields Warren, M.D. Dwight O'Hara, M.D.
C. Guy Lane, M.D. Chester S. Keefer, M.D.
William A. Rogers, M.D. Howard M. Clute, M.D.
Stephen Rushmore, M.D. Fletcher H. Colby, M.D.
Henry R. Viets, M.D. Robert L. Goodale, M.D.
Robert M. Green, M.D. Chester M. Jones, M.D
Charles C. Lund, M.D. Harvey R. Morrison, M.D.

Associate Editors

Thomas H. Lanman, M.D. Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year (Boston funds); $8.52 per year for all foreign countries belonging to the Postal Union.

Material should be received not later than noon on Thursday, two weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

## COMPENSATION FOR EMERGENCY CARE IN CASES OF INDUSTRIAL INJURY

This issue of the *Journal* carries a communication from the Secretary that deserves the notice of all the members of the Massachusetts Medical Society, particularly those who occupy regular positions on a hospital staff. Heretofore the right of staff physicians to compensation for services rendered those injured in industry has been challenged by many insurance companies. Their refusal to pay for such services was based on certain decisions of the Massachusetts Supreme Court. These decisions seem to have arisen out of the Court's interpretation of the law as it relates to hospitals and to the principle of free choice of physician as provided for in the Massachusetts Workmen's Compensation Act.

The layman reading these decisions is led to believe that the Court regards hospitals as merely asylums for the poor. Although it is true that the law frequently lags a bit behind what has come to be regarded by the people as established social practice, it seems incredible that it should lag so far behind as not to recognize what everybody, for a long time, has come to accept as the hospital's function in the scheme of American life. The present-day hospital serves the whole community without any loss of emphasis on its original purpose. It has done this as the result of public demand, in keeping with scientific progress and a changing way of life.

The Workmen's Compensation Act was established for the purpose of protecting the workman and his family from the hazards of industry. When the workman ran afoul of these hazards, the responsibility for his care was placed by law on industry itself, as a legitimate addition to the costs of production. It is little wonder, then, that many physicians are bewildered by these decisions of the Court, which put doctors in the position of sharing costs that are imposed elsewhere by the law. Mrs. Tousant, the able chairman of the Massachusetts Industrial Accident Board, has expressed, in conference with the Committee on Public Relations of the Society, the Board's dissatisfaction with the way in which many industrial injuries have been handled. She is agreed that the confusion caused by the issues discussed here may be partly responsible.

The agreement reported elsewhere in this issue is the result of many conferences held by the Massachusetts Industrial Accident Board with the Medical Advisory Committee of the Board, a subcommittee of the National Council of Claims Executives on Compensation Insurance and a subcommittee of the Committee on Public Relations of the Massachusetts Medical Society. Drs. Daniel J. Ellison, David D. Scannell and Gordon M. Morrison, who comprise the latter subcommittee, deserve the sincere thanks of the Society.

This agreement has done much to clear the air, and it is the obligation of every hospital-staff physician to see to it that the confidence of the Industrial Accident Board has not been misplaced.

## SHORTAGE OF NURSES STILL ACUTE

Following a summer in which the war news became increasingly good, the needs of the military services for nurses have grown steadily more acute. The victories that are winning the war are taking their toll, on every front, in casualties. All the nurses actively taking part in the combat areas abroad and in the military hospitals at home and many of those in other types of foreign service are reaching the point where they themselves need relief. With the present plan for releasing those who cannot continue under the strain and for giving leave to those who have had long stretches of service, the need for additional enlistments continues.

According to official reports, the New England states were 120 short of meeting their quota of 1023 for the first half of the year, although both Massachusetts and Rhode Island went well over their state quotas. They are now asked to provide 1000 more nurses during the last part of 1944, at least half of them by November 1. The Massachusetts quota — 526 — is naturally the largest.

Most of these enlistments must come from new and recent graduates. It is expected that at least 30 per cent of the new graduates from the schools of nursing will be available for military service, 50 per cent for essential civilian service, and perhaps 15 per cent — those specially qualified — for postgraduate study. No recent graduate will be fulfilling her professional obligation at this critical time if she enters private-duty nursing or office nursing, both of which must be cut to the minimum until the acute shortage is relieved.

Although some institutions and agencies seem to have weathered their worst periods of shortage, others find things more and more difficult with each passing month. This is particularly true of some of the hospitals without schools of nursing, which are in extreme need of head nurses, supervisors and nurses for the general staff. If, as now seems apparent, the general military hospitals, such as the Cushing, the Lovell and the Edwards, here in Massachusetts are also going to need civilian nurses for the next few months to supplement the staff of Army nurses, then there is no likelihood that the efforts to see that nursing service is equitably distributed to meet the most essential needs can be relaxed.

It is important for every physician to know the situation and to use his influence to restrict the use of nurses in private cases or noncritical office work until the needs of the armed forces and civilian hospitals are adequately met.

---

## MASSACHUSETTS MEDICAL SOCIETY

### SECRETARY'S OFFICE

It seems important that those of our members who occupy staff positions in Massachusetts hospitals should have called to their attention in this special manner an agreement that has just been concluded through the aegis of a subcommittee of the Massachusetts Medical Society appointed to confer with the Medical Advisory Committee of the Industrial Accident Board. The subject on which this agreement has been reached has been a source of contention over the years. The elimination of this contention should pave the way for better care of those injured in industry and for a better understanding between all concerned.

The report of Drs. Daniel J. Ellison, David D. Scannell and Gordon M. Morrison, which ably and clearly set forth this agreement and the manner in which it may be maintained, is as follows:

> This report is a follow-up in a matter on which a preliminary report was made one year ago.
>
> This committee was appointed at the request of the Industrial Accident Board to recommend procedures whereby the medical care and surgical care of the injured workman might be improved. It was and still is the opinion of this committee that the surgical staffs of recognized hospitals, by and large, represent the men in any given community most able to cope with surgical conditions.
>
> Our first procedure was to attempt to make these men more willing to care for or handle industrial accident cases while they were on duty on ward service. To this end, through the co-operation of the chairman of the Industrial Accident Board, it has now been agreed by all the insurance companies handling this type of business that the man rendering emergency treatment to an injured workman shall be paid for such treatment. In defining first-aid treatment it may be said that emergency treatment ranges from simple first-aid to an extensive operation for the relief of a compound fracture. Reasonable charges submitted by any registered physician in this state will be honored. There shall be no change in the relation between the patient and the hospital-staff physician as it now exists in the various hospitals of the Commonwealth. The problem of the surgeon on duty caring for an injured employee in the ward without being paid except for the emergency treatment cannot be solved by any method except the passage of an amendment to the law by the General Court providing for the payment for such services or a reversal of the ruling previously made by the Supreme Court. It is the opinion of the committee that, whereas surgeons on ward service render equally as able care to both ward and private patients, it might be well to institute proceedings that would change this rather unfortunate state of affairs.
>
> Payment will not be made for services rendered by interns or residents but for work actually done by surgeons

recognized by a hospital, whether or not on duty. This we believe to be a step forward in the better care of the injured workman.

It is also agreed that the injured employee, if conscious, shall be offered two lists of physicians, — one a list of staff doctors selected by the insurer and the other a complete list of the members of the hospital staff, including the courtesy staff, — with the understanding that the employee has a free choice of any doctor on either of these lists. On the other hand, should the injured employee choose as his physician a doctor connected with some hospital other than the one to which he has been taken he may be removed without prejudice to that hospital, where the physician of his choice may care for him.

Your committee believes that it is impossible to prevent a certain number of these patients being taken to unaccepted hospitals and being cared for by men of limited ability, but that the solution of this part of the problem lies in an educational program designed to teach people the difference between recognized and unrecognized hospitals. The problem is not so simple as it seems at this time owing to the absence of many of the best men in the service and to the fact that their places have been taken by men of considerably less maturity in judgment.

There is one other arrangement that has recently been concluded that in some cases may obviate this difficulty. Through an agreement with the Blue Cross, an injured employee insured under the Blue Cross may be transferred from a ward to a semiprivate or private room and the difference in expense will be paid by the Blue Cross, making such an employee the private patient of the surgeon on duty or of the surgeon chosen by the employee.

It is further thought that freedom of choice of physician by the injured employee should at no time be interfered with.

It is the desire of the chairman of the State Industrial Accident Board that a committee of this type be continued.

This agreement should be studied carefully, and every assistance should be given to Massachusetts hospitals by their respective staff members in putting its provisions into practice.

The Industrial Accident Board has already addressed the hospitals in this same vein.

MICHAEL A. TIGHE, *Secretary*

---

## DEATHS

FAULKNER — Herbert K. Faulkner, M.D., of Keene, New Hampshire, died September 15. He was in his eighty-sixth year.

Dr. Faulkner received his degree from Harvard Medical School in 1885 and practiced in Keene for forty years before retiring in 1920.

Five daughters and two sons, one of whom is Captain James M. Faulkner (MC), U.S.N.R., survive.

---

OUTHOUSE — John S. Outhouse, M.D., of Shelburne Falls, died June 20. He was in his seventieth year.

Dr. Outhouse received his medical degree from McGill University, Montreal, in 1898.

His widow, one daughter and two grandchildren survive.

---

SHERMAN — Frank M. Sherman, M.D., of West Newton, died September 14. He was in his eighty-eighth year.

Dr. Sherman received his degree from Harvard Medical School in 1881. He had retired several years ago.

His widow, two sons and a daughter survive.

# MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

## CONSULTATION CLINIC FOR CRIPPLED CHILDREN

| CLINIC | DATE | CLINIC CONSULTANT |
|---|---|---|
| Salem | October 2 | Paul W. Hugenberger |
| Haverhill | October 4 | William T. Green |
| Lowell | October 6 | Albert H. Brewster |
| Pittsfield | October 16 | Frank A. Slowick |
| Springfield | October 18 | Garry deN. Hough, Jr. |
| Brockton | October 19* | George W. Van Gorder |
| Worcester | October 20 | John W. O'Meara |
| Fall River | October 23 | Eugene A. McCarthy |
| Hyannis | October 24 | Paul L. Norton |

*Date changed.

---

# WAR ACTIVITIES

## INDUSTRIAL HYGIENE

### A HEALTH PROGRAM FOR SMALL INDUSTRIES

A campaign for the advancement of industrial health in the small industries of the Detroit area is being sponsored by the Wayne County Medical Society. The main objective is to provide emergency care in these plants and eventually to convince the management that a health program is not costly but economically profitable, even though it necessitates an initial expenditure for first-aid stations and certain equipment.

When a sufficient number of doctors have notified the society of their availability to assist in the program, letters will be sent by the medical society to industries in the area employing 25 to 1000 workers that do not employ a full-time plant physician. The City of Detroit Department of Health has offered to render service or advice regarding occupational diseases found in these plants.

The plan proposes meetings at regular intervals, in each plant, of the president or plant manager, the plant doctor or his appointed representative, the plant or visiting nurse, the first-aid man, the director of the safety committee, a representative of the employees and the personnel or employment manager. Suggested topics for these meetings include: disabilities from accidents; first-aid at the plant; physical examination and health of the worker; noncompensable illnesses such as colds, other infections and surgical disabilities; co-operation of the family physician in cutting down loss of workdays; ventilation and sanitary conditions in the plant; nutrition of the workers and food conditions; and contagious diseases and co-operation with the public-health department. — Reprinted from *Industrial Hygiene News Letter* (August, 1944).

---

# CORRESPONDENCE

## CASH BENEFITS

*To the Editor*: The editorial "Massachusetts EMIC Program" in the September 7 issue of the *Journal* was interesting and timely. It called to mind an editorial appearing in the January 20, 1938, issue of the *Journal*, entitled "Group Health Association, Incorporated." That editorial questioned the wisdom of the American Medical Association's opposition to Group Health Association, Washington, D. C., and suggested that the manner in which the medical profession reacted to medical-service plans was of vital importance to physicians. The subsequent decision of the Supreme Court of the United States concerning the opposition of the American Medical Association and the unfortunate publicity that accrued to the medical profession seem to have amply supported the former editorial comment.

In the present instance the American Medical Association has again taken action that may be detrimental to physicians. It has recommended that the cash allotment method of dis-

bursing funds under the EMIC program be substituted for the present method of directly paying physicians for the services they render. The advocacy of such cash benefits by the profession may lead the public to believe that physicians approve the expenditure of the public's money under the pretext of medical care without concern whether or not that money is actually spent on medical care. The public may also infer that the profession is not concerned about the quality of medical care purchased with government funds. Finally, the public may conclude that doctors wish to be in a position to negotiate with each of these mothers the fees that they should pay and thus disregard the decision of Congress to free such mothers from the worries of medical expense.

If the public should feel that doctors are more concerned with protecting the present system of medical practice than in economically distributing the cost of medical care and improving its quality, then the public is likely to pay little attention to the advice of the profession in the consideration of programs for the improvement of medical care. Thus it would seem that the advocacy of cash benefits by the official bodies of the medical profession is a matter of importance to physicians, for they suddenly may find that their official representatives have once again subjected the medical profession to public criticism.

ALLAN M. BUTLER, M.D.
Massachusetts General Hospital
Fruit Street
Boston 14

## BOOK REVIEWS

*Psychiatry in War.* By Emilio Mira, M.D. 8°, cloth, 206 pp., with 6 figures. New York: W. W. Norton & Company, Inc., 1943. $2.75.

Mira, a former professor of psychiatry in Barcelona, served during the Spanish Civil War as an active physician in the treatment of mental diseases in the Republican Army. His account is by far the best that has been written on psychiatry during this war and is of outstanding value because of its clear picture of the effects of war on the mind of man. The book forms a fitting introduction to the treatment of the many neuropsychiatric problems that are appearing in World War II, and this timely contribution will be welcomed by all physicians who have to do with the care of the American soldier mentally disturbed by war conditions. There are excellent chapters on the effect of bombing on the civilian population, in addition to the case histories and personal experience of the author at the front. The morale of an army under stress is given particular consideration.

The author is well known in this country, having delivered addresses here in 1933 and more recently being the Salmon Lecturer at the Academy of Medicine, New York City. The book comprises the latter lectures, plus additional material, particularly on the diagnostic apparatus devised by the author for estimating the fitness of a person to serve in the Army. This apparatus, which Mira believes is an efficient means of military selection, is now being used for investigation in this country.

The book is an important landmark in military psychiatry for it contains material not found elsewhere. It is well written and factual, and the conclusions should have a wide field of application both in military and in civilian life.

*The Conquest of Epidemic Disease: A chapter in the history of ideas.* By Charles-Edward A. Winslow, Dr.P.H. 8°, cloth, 411 pp. Princeton, New Jersey: Princeton University Press, 1943. $4.50.

This volume may well be considered a classic. It approaches the problem of the history of the attack on epidemic diseases with a point of view that differs from other writings. In part it is medical history; in part an anthology of the writings of the makers of that history; and in part the clear thinking of C.-E. A. Winslow. The author has attempted to depict how the leaders of medical science visualized their problems. So far as possible he has told their story in their own words, and has so woven them into the text that at times, without quotation marks, it is difficult to separate the original writer from his historian. The field of epidemic disease is unfolded from the days of the Old Testament down through the ages to Charles Value Chapin. Fracastorius, Rush, Panum, Budd, Snow, Pasteur, Koch and many others are reviewed by their thoughts rather than by their acts.

Winslow calls his work "a chapter in the history of ideas." It seems more than that. The ideas of the masters are integrated and interpreted by a master. This volume is not a textbook and may not be suited to the library of the entire medical profession but it will be a delight to those interested in medical history, to those trying to learn more regarding human understanding, to the busy doctor desirous of spending a quiet evening before the fireside and to a limited number of public-health workers, both medical and nonmedical.

*The Genealogy of Gynaecology.* By James V. Ricci, M.D. 4°, cloth, 578 pp., with 53 illustrations. Philadelphia: The Blakiston Company, 1943. $8.50.

This is an authoritative, scholarly and well-documented history of gynecology from its remotest archaic beginnings through the Assyrian, Babylonian, Egyptian and Hindu epochs, the classic Graeco-Roman age, the Talmudic, Byzantine and Arabic eras and the Middle Ages and Renaissance to the end of the eighteenth century. From all these epochs there is an abundant bibliography and the reproduction of fifty-three well-selected illustrations, chiefly of gynecologic instruments and of developing anatomical concepts. In his preface, as in his gracious dedication to the Harvard Medical School, the author freely acknowledges his indebtedness to previous writers but modestly underestimates the wide-ranging and painstaking research that the accumulation of his material must have required. His work is a priceless gift to the profession, and one waits with eager anticipation for the subsequent volume, promised in the introduction by Dr. Schumann, of Philadelphia, covering the period of the nineteenth century.

*Reaction to Injury: Pathology for students of disease based on the functional and morphological responses of tissues to injurious agents.* By Wiley D. Forbus, M.D. 4°, cloth, 797 pp., with 532 illustrations, 20 of which are in color. Baltimore: Williams & Wilkins Company, 1943. $9.00.

Forbus's new textbook of pathology follows the arrangement that has been made familiar by MacCallum's book — an etiologic compilation based on the type of injury causing disease. The present volume contains introductory material, a brief chapter on the history of pathology, a classification of the causes of disease and a full discussion of infectious diseases. The author states that a second volume covering the other fields of pathology is in preparation but that the importance of infectious diseases in wartime makes the publication of the first volume worth while at the present moment.

The discussion of the topics within the scope set for the work as it now stands is more complete than in most pathology texts, such as those of Boyd and Karsner. The presentation of material is clear and critical; both sides of controversial questions are given, and dogmatic statements are meticulously avoided. The pathology of the various infectious diseases is set in relation to the picture of the diseases as wholes, and an adequate basis for the difficult transition from preclinical to clinical studies is provided. This has been accomplished to a certain extent at the sacrifice of considerations of disease as a biologic phenomenon, particularly in its relation to biochemistry.

There are many advantages in the arrangement of a text according to the type of injury causing disease. These accrue chiefly from the fact that etiology receives the emphasis that it deserves, yet it often separates by hundreds of pages subjects that should be considered together. For instance, Forbus discusses glomerulonephritis among the acute and chronic, nonsuppurative inflammatory processes, whereas vascular diseases of the kidneys will be considered in the volume that has not yet appeared. "You pay your money and take your choice."

The illustrations are definitely superior to those of most texts of pathology now in general use. The photographs of gross specimens are excellent, as are most of the photomicrographs. Some of the latter could be improved by procuring better fixed and stained preparations (for example, Figs. 309,

343, 345 and 508). The colored plates are made from Kodachromes of varying merit.

References follow each chapter. These are well chosen from the student's viewpoint but are considerably out of date, few of them being more recent than four years before the publication of the volume. In some instances, later material is included in the text than in the bibliography.

Within the fields covered by this volume, the text is one of the best now available. It will appeal to the better students, which is as it should be, and to those clinicians and pathologists who wish a reference work on the pathology of infectious diseases. Forbus's book is a welcome change from the numerous textbooks of pathology that are little more than catalogues of disease. Without supplementation by another text, it lacks too many important topics (for example, arteriosclerosis and tumors) to make it suitable for a second-year course in pathology as it stands.

## BOOKS RECEIVED

**The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.**

*Office Treatment of the Nose, Throat and Ear.* By Abraham R. Hollender, M.D., associate professor of laryngology, rhinology and otology, University of Illinois College of Medicine, and otolaryngologist, Research and Educational Hospitals, Chicago. 8°, cloth, 480 pp., with 33 illustrations. Chicago: The Year Book Publishers, Incorporated, 1943. $5.00.

This manual is written for the purpose of furnishing details of office treatment not usually found in prescribed college curriculums or in the training provided for residents in hospitals. The work is divided into two sections: the first discusses the general therapeutic methods used in all diseases of the upper respiratory tract, and the second considers the various diseases of the nose, sinuses, mouth, larynx and ear.

*The Religious and Philosophical Aspects of van Helmont's Science and Medicine.* By Walter Pagel. 4°, paper, 44 pp. Baltimore: The Johns Hopkins Press, 1944. $1.00.

In this monograph an attempt is made to define the position of van Helmont in the history of philosophy.

*Safe Convoy: The expectant mother's handbook.* By William J. Carrington, M.D., attending gynecologist, Atlantic City Hospital, Atlantic County Hospital for Nervous and Mental Diseases, Pine Rest Hospital, Atlantic City Municipal Hospital and Atlantic Shores Hospital. 8°, cloth, 256 pp. Philadelphia: J. B. Lippincott Company, 1944. $2.50.

This manual of personal hygiene for the expectant mother has been written by an obstetrician of large experience. One third of the volume is devoted to the care of the newborn infant. The foreword comprises a short history of obstetric books for the laity.

*Minor Surgery.* By Frederick Christopher, M.D., associate professor of surgery, Northwestern University Medical School, Chicago, and chief surgeon, Evanston (Illinois) Hospital. Fifth edition. 8°, cloth, 1006 pp., with 575 illustrations. Philadelphia and London: W. B. Saunders Company, 1944. $10.00.

The text of this edition has been thoroughly revised; many sections have been entirely rewritten, and many new sections have been added. The subjects of wound healing and treatment have been rewritten with particular attention to the local use of sulfonamides, and the administration of penicillin is discussed. The employment of plastic casts in wound treatment is considered. The section on burns has been extensively revised and includes consideration of the use of nonadherent pressure dressings and of plasma administration. A new chapter on preoperative and postoperative care has been added. This includes the following topics: shock and its treatment with blood plasma and other agents; dehydration; hypoprothrombinemia; vitamin deficiency (including vitamin K); preoperative preparation in special cases; water balance; electrolyte requirements; protein requirements and treatment of hypoproteinemia with amino acids; the use of the Miller–Abbott tube; postoperative pulmonary complications; prophylaxis and treatment of postoperative thrombosis and embolism (including the use of heparin and dicumarol); and postoperative urinary complications (including the use of sodium lactate to increase the pH of the urine during administration).

New subjects considered or emphasized for the first time are tetanus toxoid, new developments in the treatment of varicose veins, ligation of the femoral vein in thrombophlebitis, treatment of pilonidal sinuses, wire sutures in tenorrhaphy, the hanging cast in fractures of the humerus, x-ray treatment for sprained ankles, "paratrooper fracture," walking casts, sternal infusions, treatment of cardiac arrest and employment of intravenous anesthesia.

This authoritative treatise, first published in 1929, should prove of great value at the present time to physicians who are called on to treat minor surgical conditions.

*The Hippocratic Oath: Text, translation and interpretation.* By Ludwig Edelstein. A supplement to the *Bulletin of the History of Medicine.* 4°, paper, 64 pp. Baltimore: The Johns Hopkins Press, 1943. $1.25.

The text of the oath is given in both Greek and English. In his interpretation Dr. Edelstein has scrutinized the text, sentence by sentence, and has made extensive use of the writings of ancient authors in his inquiries. The covenant, which precedes the code, and the ethical code are considered separately. The two final chapters discuss the unity of the document and the date and purpose of the oath. This scholarly presentation should be on the shelves of every library.

*Health for the Having: A handbook for physical fitness.* By William R. P. Emerson, M.D., medical consultant in physical fitness, Aetna Life Insurance Company. 12°, cloth, 146 pp., with 6 illustrations. New York: The Macmillan Company, 1944. $1.75.

This small manual has been written for the layman, and much emphasis is placed on body weight and personal hygiene. Correct diet is stressed and valuable tables of calories and weight and height are appended to the text.

*Physical Foundation of Radiology.* By Otto Glasser, Ph.D., professor of biophysics and head of Department of Biophysics, Cleveland Clinic Foundation, Cleveland; Edith H. Quimby, Sc.D., associate professor of radiology (physics), College of Physicians and Surgeons, Columbia University, New York; Lauriston S. Taylor, Ph.D., chief of X-ray Section, National Bureau of Standards, Washington, D.C.; and J. L. Weatherwax, M.A., Philadelphia General Hospital and Graduate School of Medicine, University of Pennsylvania, Philadelphia. 12°, cloth, 426 pp., with 95 illustrations and 53 tables. New York: Paul B. Hoeber, Incorporated, 1944. $5.00.

This combined work of four authors is an attempt to provide a teaching text in the field of radiologic physics. The manual has been designedly written in an elementary and nonmathematical character. General bibliographies and special references are appended to each chapter for the purpose of furnishing material to teachers who may desire to supplement the text with other material. Throughout the book the place of radiologic physics as a part of modern physics has been kept in mind. There is a special chapter on therapy records, which is amplified by extensive tables of dosage data for both x-rays and radium. The first chapter, which is historical, contains valuable chronologies from the time of Gilbert in 1600 to Kerst in 1940. These tables make the manual invaluable to all those interested in the history of medicine and physics. The book is well printed with a good type and is of a convenient size to handle.

## NOTICES

### TUFTS POSTGRADUATE COURSES FOR THE GENERAL PRACTITIONER

The Postgraduate Division of Tufts College Medical School has recently announced a series of courses designed for the busy general practitioner who wishes to bring his knowledge up to date. The work is largely given in the New England

Medical Center (Boston Dispensary, Joseph H. Pratt Diagnostic Hospital, Boston Floating Hospital and Tufts College Medical School). Facilities of other hospitals in and around Boston are also available in several of the courses.

Graduates of approved medical schools are eligible for admission to any of the courses. Graduates of other medical schools may be admitted if considered acceptable. Such applicants should submit evidence that they are members of their state medical societies. Applications for admission and requests for further information should be made to the Chairman, Postgraduate Division, Tufts Medical School, 30 Bennet Street, Boston.

Tuition fees are payable on the opening day of each course. In addition, a $5.00 registration fee covers all courses taken within a twelve-month period and is due on acceptance for study. The registration fee will be forfeited in cases of withdrawal without notification.

Through the Bingham Associates Fund, fellowships for postgraduate study are available for physicians practicing in Maine who are members of the Maine Medical Association. Application should be made to the Chairman. These fellowships are not available to physicians from other parts of New England; the tuition fees, however, are placed at a level calculated to make the courses available to the great body of physicians in New England.

For a limited number of physicians, room and board are available at the New England Medical Center. Rates for room are $10.00 double and $12.00 single per week. Meals are available through the purchase of meal tickets. Reservations for room accommodations *must be made* in advance and should be addressed to Mr. Frank E. Wing, Director, Boston Dispensary, 25 Bennet Street, Boston.

## AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

A number of changes in regulations and requirements were put into effect at the last annual meeting of the American Board of Obstetrics and Gynecology. These were designed to aid civilians as well as candidates in the service. Among these is the waiver, temporarily, of the requirement of the American Medical Association for men in the Army or Navy, especially for those who proceeded directly or almost so from hospital into military service, on a statement of intention to join promptly on return to civilian practice. At this meeting the Board also decided to accept a period of nine months as an academic year in satisfying the requirement for certain years of training. This is only for the duration and even men who are not eligible for military service but who are nevertheless in hospitals where the accelerated program is in effect have been allowed to submit this short-time period of training in lieu of the previous requirements.

Beginning with the next written examination, which is scheduled to be held on the afternoon of February 3,1945, the Board will limit the written examination to a maximum period of three hours, and in submitting case records, all obstetric reports that do not include measurements, either by calipers and, as indicated, by acceptable x-ray pelvimetry, will be considered incomplete.

Prospective applicants or candidates in military service are urged to obtain from the office of the Secretary a copy of "Record of Professional Assignments for Prospective Applicants for Certification by Specialty Boards," which will be supplied on request. This record was compiled by the Advisory Board for Medical Specialties and is approved by the offices of the Surgeons-General, having been recommended to the services in a Circular Letter No. 76 from the War Department Army Service Forces, and referred to as the "Medical Officer's Service Record." These will enable prospective applicants and candidates to keep an accurate record of work done while in military service and should be submitted with the candidate's application, so that the Credentials Committee may have this information available in reviewing the application.

Applications and a bulletin of detailed information regarding the Board requirements will be sent on request to the Secretary's Office, 1015 Highland Building, Pittsburgh 6. Applications must be in the office of the Secretary by November 15, 1944, ninety days in advance of the examination date. The time and place of the Spring 1945 (Part II) examination will be announced later.

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, October 5, in the classroom of the Nurses' Residence at 7:15 p.m. A motion picture on caudal anesthesia will be shown. Dr. Mabelle C. Hiscock will be chairman.

## SOCIETY MEETINGS AND CONFERENCES

### Calendar of Boston District for the Week Beginning Thursday, October 5

Thursday, October 5
7:15 p.m. New England Hospital for Women and Children.

Saturday, October 7
*10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

Monday, October 9
*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

Tuesday, October 10
*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

Wednesday, October 11
*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

October 2–5. Second Wartime Public Health Conference. Page 436, issue of September 21.

October 2–7. Seminar in Legal Medicine, Harvard Medical School. Page 110, issue of July 20.

October 3–5. American Public Health Association. Page ix, issue of March 30.

October 9–20. 1944 Graduate Fortnight of the New York Academy of Medicine. Page xvii, issue of July 27.

October 10. New England Society of Anesthesiology. Page xvii, issue of September 7.

October 13. Mental Conditions Resulting from the War. Dr. C. A. Bonner. Pentucket Association of Physicians. 8:30 p.m., Haverhill.

October 16–November 3. Third Postgraduate Course in Industrial Medicine. Page xix, issue of September 14.

October 30. New York Institute of Clinical Oral Pathology, New York Academy of Medicine. Page 110, issue of July 20.

November 2–4. Association of Military Surgeons. Page xiii, issue of August 17.

February 19. American Board of Internal Medicine. Page 436, issue of September 21.

### District Medical Societies

SUFFOLK

December 7. Censors' meeting.

WORCESTER

October 11. Rutland State Hospital.
November 8. Grafton State Hospital.
December 13. Worcester City Hospital.
January 10. St. Vincent Hospital, Worcester.
February 14. Worcester State Hospital.
March 14. Worcester Memorial Hospital.
April 11. Hahnemann Hospital, Worcester.
May 9. Annual meeting.